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Public Health

The order in this section is:—General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.

VITAL STATISTICS

DREYER, Karen & NØRREGAARD, S. **Causes of Late Foetal Death in Denmark 1955-1957.** *Danish Med. Bull.* 1960, Oct., v. 7, No. 5, 145-52.

The death certificates relating to 3,922 late foetal deaths occurring during 1955-57 have been analysed in detail in an attempt to outline the problems presented by these deaths and to see whether further information should be obtained. In Denmark, as in other countries, a definite cause cannot be assigned to a large proportion of these deaths and in others with several pathological conditions it is difficult to say with certainty the one responsible for death. In Denmark two kinds of certificates are in use for stillbirths, one issued by the midwife and one by the doctor, the latter is only compulsory in the towns. Death occurred before delivery in 44.5% of the deaths, during delivery in 29.6% and in 25.9% the time of death was unknown. The largest causes of death were diseases of foetus and ill-defined causes, 36.6%, placenta and cord conditions, 29.7% and difficulties in labour, 14.1%. Male deaths predominated in the figures for most causes although only 40.5% of the 363 deaths due to congenital

malformations were of males; this low proportion was due to anencephalus, to which deaths of 100 females and 30 males were attributed. A comparison with some other countries for which data are available showed some interesting contrasts. The rate for toxæmia in Denmark is about one-quarter of the rate in New Zealand but the rate for maceration, cause not defined, was about 9 times higher in Denmark than in New Zealand. Congenital malformation of the foetus was an important cause of death in Scotland, the rate being about 3 times that of Denmark and twice that of other countries in the comparison.

The authors conclude that an improvement in Danish death certificates for late foetal deaths is called for and, not least, a change in the doctor's attitude towards this problem.

W. J. Martin

BAILEY, M. J. **Factors associated with Variations in Maternal Death Rates.** *Human Biol.* 1960, Sept., v. 32, No. 3, 274-87.

MATERNAL AND CHILD HEALTH

STAHLIE, T. D. **The Natural History of Pregnancy and Childbirth in Thailand.** *Trop. & Geograph. Med.* 1960, June, v. 12, No. 2, 127-37, 1 fig.

Data about pregnancy and labour were obtained from reports and from interrogation of 1,755 women in 7 areas of Thailand concerning their 2,349 pregnancies. The findings were supported by the findings in Bangkok Midwifery School. They demonstrate that whereas in western countries toxæmias and abnormal presentations are the main problems, in Thailand defective nutrition dominated the picture and abnormal presentations and obstructed labour were unusual or rare. Uncommon complications of pregnancy were hyperemesis, toxæmia,

diabetes, macrocytic anaemia and deficiency diseases other than beriberi. Common conditions were microcytic anaemia and beriberi which had an average incidence of about 10% in pregnant women. Clinical syphilis was rare but positive serological tests were common, possibly owing to latent yaws. A mild antepartum haemorrhage occurred in under 1%, probably owing to partial placenta praevia, possibly aided by beriberi. Pregnancies in very young or old women were rare. The period between pregnancies was about 3 years, probably because of prolonged lactation rather than birth control.

Post-partum haemorrhage, usually not severe, was common, reaching an incidence of 23% in areas of serious nutritional deficiency. The cause was probably an atonic

uterus affected by beriberi, and not a retained placenta. Puerperal fever incidence varied between 1% and 8.5% but a proportion was probably malarial. The custom in rural areas of the mother spending days, or even weeks, of the early puerperium swaddled in heavy clothing or close beside a large fire, without food other than rice and salt water, tends to cause beriberi. The most urgent need in Thailand is thus the provision of a good diet and education of the mother in nutrition. *T. H. Davey*

SEEDORF, H. H. **Is Prophylactic Treatment of the Eyes of Newborn Infants still Necessary?** *Danish Med. Bull.* 1960, Oct., v. 7, No. 5, 128-32, 2 figs. [28 refs.]

According to the wish of the Danish National Health Service and on the initiative of the heads of the hospital concerned, the two maternity departments of the Rigs-hospital in Copenhagen underwent the following tests: As from December 1, 1958, one of them, Department A, discontinued for a year the routine instillation of silver nitrate into the eyes of the newborn. Department B, with the same number of deliveries, and the same social class of patient, continued this silver nitrate service as before. All the infants in A were examined twice by an ophthalmologist, once within the first 3 days of life, and once just before discharge from hospital. On the appearance of physical signs of conjunctival infection, the nurses took swabs from the conjunctival sac for the typing of the bacteria found. Smears were taken on the same day in a search for intracellular diplococci. If found, antibiotic treatment was started at once. 7 cases of gonococcal conjunctivitis occurred in A, whereas there was not one such case in B. There were also 80 cases of non-specific conjunctival infection in A, whereas there were only 9 such cases in B. Hence the conclusion that prophylactic instillation is still necessary despite an improved venereal disease legislation and the introduction of chemotherapy. The present study was not concerned with the comparative merits of silver nitrate and antibiotics, but it would seem that there is insufficient evidence at present to warrant the replacement of the former by the latter in this particular field. *Claude Lillingston*

COOK, N. J. **The First Year of Life.** *Med. Officer.* 1960, Oct. 7, v. 104, No. 15, 219-25. [17 refs.]

This is a study of 222 boys and 202 girls under the care of one general practitioner paediatrician. Registration with the practice did not usually occur before the infants were aged 3 to 4 weeks. Hence there were few purely neonatal conditions recorded: there were 2 deaths;

one from pneumonia and the other from an obscure liver disease.

The average number of illnesses per child and the average number of visits paid have been calculated: the former is regarded as a measure of incidence and the latter of severity. The average number of illnesses for which the doctor was consulted was 4.25 for boys and 4.03 for girls: the boys received an average of 4.36 visits and the girls 3.81: apart from routine attendances at the Infant Welfare Clinic conducted by the practice the boys made an average of 4.64 attendances and the girls 4.35.

A table gives the principal illnesses recorded: 52.59% were respiratory; 14.81% illnesses of the nervous system and special sense organs (mainly otitis media and conjunctivitis); 11.40% digestive (diarrhoea and teething); 8.72% skin (one-third napkin dermatitis) and 3.30% specific infectious diseases.

January was the month with the highest incidence of illnesses. The total illness incidence did not vary significantly with the months when the babies were born. The first-born in a family had slightly fewer illnesses than the second or third and the number of visits paid was more for the third and fourth babies than for the first and second.

When analysed by social class the average illnesses per child were 3.71 for Classes I and II combined, 4.22 for Class III, 4.06 for IV and 4.28 for V but more visits were needed for Class V indicating that the illnesses were more severe.

The illnesses per child recorded in this survey are higher than in any previous survey made in Britain and the reasons are discussed briefly. One is that this practice has its own Infant Welfare Clinic and minor ailments discovered there have been included in the survey; however, 135 of the 424 children never attended the clinic and though they had a lower than average number of illnesses they had more than the average number of home visits.

The records on the duration of breast feeding are incomplete but, in general, the wholly breast-fed had fewer illnesses than the wholly bottle-fed.

Acute bronchitis and bronchopneumonia were more prevalent among boys than girls. Lower respiratory infections were commoner in the lower income groups and in homes where cleanliness was not evident. Gastro-enteritis was more prevalent in winter than in the other seasons and among breast- than bottle-fed babies.

There were only minor differences in the average number of illnesses between the infants of under, average or over weight at birth.

A general impression is that boys are more susceptible than girls to unfavourable social factors.

Many unexpected facts emerge from this detailed, intensive and admirable study but, as the author says, the number of babies studied is "too small to support any hypotheses at present".

Allen Daley

CHRONIC CARDIO-RESPIRATORY DISEASES

CANDIOTTI & MOINE, M. Étude comparative des décès par maladies cardio-vasculaires enregistrés, en 1955, en France et dans certains pays étrangers. [Comparative Study of Deaths from Cardiovascular Diseases Registered in France and Certain Other Countries in 1955] *Bull. Inst. Nat. Hyg. Paris*. 1959, July-Aug., v. 14, No. 4, 829-54, 10 figs.

The authors have examined the crude death rates in 1955 from cardiovascular disease, in France and 17 other western countries including the United States, Canada, Australia and New Zealand. The highest rates are found in the British Isles and in Austria, and are nearly equal for each sex. The next highest male death rate is in the white population of the United States, but the rate for females is only about three-quarters of the male rate. In 6 of the 12 European countries the male rate exceeds the female rate, and in the remaining 6 the reverse is true. The United States and the 3 British dominions show a marked preponderance of male deaths.

The total cardiovascular death rates have then been broken down into the more detailed groups of the "A" international list. England and Wales and Scotland have among the highest rates for vascular lesions of the central nervous system (A 70), for chronic rheumatic heart disease (A 80), and for arteriosclerotic and degenerative heart disease (A 81). France shows very low rates for these last two categories, but outstandingly high rates for other heart disease (A 82). She has rather low rates in each sex for cardiovascular disease as a whole, the only countries with lower figures being Holland, Norway and Italy.

From the great excess in France of deaths allocated to other heart disease, not reflected in the total cardiovascular death rates, the authors have inferred that French methods of death certification are imprecise compared with other countries. They have made a further assumption, that many deaths allocated in France to undefined causes (Category 45 of the short "B" international list) would in other countries have been certified as cardiovascular. For comparative purposes they have therefore assumed, emphasizing the arbitrary basis for this assumption, that at every age the same proportion of these undefined deaths should be certified as cardiovascular, as cardiovascular deaths themselves bear to all deaths of specified cause. By this interpolation the French crude death rates from cardiovascular disease for 1955, in both sexes together are augmented by 21·8%.

The corrected French age-specific rates are then compared with the corresponding rates in Holland, where the standard of death certification is particularly high. Little difference is found in any age-group between the two countries. The higher crude rate in France is thus mostly accounted for by the older average age of the population.

The age-specific death rates from vascular lesions of the central nervous system (A 70) in France have also been compared with England and Wales. The rates for each sex in both countries are nearly equal, up to and including the age-group 30-34. At older ages the British rates overtake the French, until at ages over 85 they are nearly twice as great. It is considered that these extra British deaths do not represent any real difference in

mortality experience but would have been allocated in France to an imprecise category (B 45).

Further evidence has been sought on the imprecision of death certificates in France by local comparisons. The numbers of cardiovascular deaths allocated to different causes in Paris, the Paris suburbs, the Seine Department and the whole of France were compared with the corresponding numbers of deaths certified in the Public Assistance hospitals in the Paris area. There was little decrease in the proportion of such deaths allocated to other heart disease (A 82) in the hospitals (60·5%) compared with other areas (61·3% in the Seine Department and 70·3% in France as a whole). "*Peut-on admettre comme une éclatante victoire le maigre gain que traduisent ces chiffres?*" the authors ask ironically. It was possible, however, to study a sub-group of these hospital deaths occurring in male patients who have been treated for an appreciable time in the same hospitals before death. In this group the proportion of cardiovascular deaths to all certified deaths was considerably higher than in all hospital certified deaths (57·6% compared with 13·6%), and the proportion of cardiovascular deaths allocated to other heart disease (A 82) was much lower (34·3% compared with 58·9%).

Finally, crude death rates from cardiovascular disease were analysed regionally by Departments, and striking contrasts were found. For instance, in Corsica deaths certified as due to cardiovascular disease were 105 per 100,000, while deaths from ill-defined causes were 58·9% of all certified deaths. By contrast, the Department of Haut-Rhin had a rate of 306 per 100,000, with only 8·6% of deaths in an ill-defined category. Difficulties of communication in mountainous areas such as Corsica are thought to increase the proportion of ill-defined causes of death. Cardiovascular mortality is also closely correlated with the average age of the inhabitants of an area.

The authors conclude that most international differences in the crude death rates for cardiovascular disease, as well as local and regional differences within France, can be explained by differences either in age-distribution or in the degree of precision with which deaths are certified.

A. S. Fairbairn

SPAIN, D. M. & BRADESS, Victoria A. Occupational Physical Activity and the Degree of Coronary Atherosclerosis in "Normal" Men. A Post-mortem Study. *Circulation*. New York. 1960, Aug., v. 22, No. 2, 239-42, 1 fig.

"In autopsies on 'normal' white men between the ages of 30 and 60, who died suddenly from accident, homicide, or suicide, there were no significant differences in the degree of coronary atherosclerosis in those engaged in sedentary occupations and those engaged in physically active occupations."

ACHESON, R. M. Observer Error and Variation in the Interpretation of Electrocardiograms in an Epidemiological Study of Coronary Heart Disease. *Brit. J. Preventive & Social Med.* 1960, July, v. 14, No. 3, 99-122, 6 figs.

JACK, I. & GANDEVIA, B. **Virus Studies in Chronic Bronchitis.** *Amer. Rev. Respiratory Dis.* 1960, Oct., v. 82, No. 4, 482-4.

"From 19 patients with chronic bronchitis observed for a year, 62 gargle specimens were obtained at the onset of symptoms referable to the upper respiratory

tract, together with 138 blood samples, including 'acute' and 'convalescent' specimens as well as regular quarterly samples. Virus isolation and serologic techniques failed to reveal evidence of infection with influenza A and B viruses, adenoviruses, hemadsorption or croup-associated viruses during the year of observation, in spite of clinical evidence of exacerbations of bronchitis."

CANCER

MITRA, S. & DAS GUPTA, A. **An Estimate of the Prevalence of Cancer in India.** *Bull. World Health Organization.* Geneva. 1960, v. 22, No. 5, 485-92, 3 figs.

Examination of death certificates for all the deaths registered in the Calcutta Corporation area during the years 1954 and 1955 shows that the proportion attributed to cancer was 2.6%. This compares with a figure of 6.5% which would have been obtained had the United Kingdom age specific death rate been applied to the Calcutta population. The proportion increased from 2.4% in 1954 to 2.8% in 1955, and this increase was a continuation of a trend observed since 1952. It is likely that the increase is due to improvements in diagnosis and death certification and that the present figure is an under-estimate of the true one. On the assumption that the Calcutta experience is typical of all India, it is estimated that the total number of cancer deaths in the country is approximately 200,000 per year and that the prevalence of cancer amounts to approximately 600,000 cases.

Analysis of the site distribution of the cancers shows that the commonest site was the female genital organs, followed by the liver and the throat. *Richard Doll*

PERNU, Johanna. **An Epidemiological Study on Cancer of the Digestive Organs and Respiratory System. A Study based on 7078 Cases.** *Ann. Med. Intern. Fenniae.* Helsinki. 1960, v. 49, Suppl. 33, 117 pp., 10 figs. [Numerous refs.]

In Finland two-thirds of all cases of cancer are of the intestinal and respiratory tract. An investigation of these forms of cancer in relation to the patients' diet, the use of stimulants, and the socio-economic status has here been made. The records of patients with cancer of the respiratory and intestinal tract seen in the Helsinki University Central Hospital, Department of Radiotherapy and Otology and Laryngology (1944-58), the Oulu District Hospital (1948-58), the South Saimaa Central Hospital (1955-58), the Central Hospital for Mid-Finland (1954-58) and cases notified from other hospitals to the Finnish Cancer Registry in 1957-58 were abstracted. These gave details of address, age, treatment and site and spread of tumour. Questionnaires on dietetic habits, smoking, work etc. were sent to all who were thought to

be still alive. Out of 10,104 questionnaires sent out, replies were received from 7,078 (70%). Parish Sisters were asked to distribute similar questionnaires "to as aged subjects as possible, who, as far as was known, were free from cancer". 4,437 questionnaires of this nature were sent out, 39.7% were returned. Figures for the age-distribution of the types of cancer collected are given. It was found that cancers of the stomach and intestinal tract were commoner in patients who had a meat and high animal fat diet, while patients with irregular meal times were more prone to oesophageal cancer. Tumours of the buccal cavity and stomach were associated with pipe smoking. Cigarette smoking was associated with cancer of the respiratory system, particularly lung and larynx. Heavy drinkers had a higher incidence of lung and oesophageal cancers (but the majority of patients who smoked also drank). Patients who gave a past history of having had the Plummer-Vinson syndrome had more cases of buccal cancer than others, cancer of the stomach was commoner in patients who had had gastritis and gastric ulcers. Bronchitis and pneumonia had a significant effect on cancers of the lung and larynx. Gastric cancer was particularly found in the lower socio-economic groups; cancer of the buccal cavity was the commonest type found in women of the lower classes, in men of the same group, cancer of the pharynx.

[This study suffers from the poor response rate, and it is dangerous to draw conclusions from samples that may be unrepresentative of the populations at risk.]

W. W. Holland

HILLIS, B. R. & CAMERON, J. A. **Observations on 100 Cases of Bronchial Carcinoma in a Rural Area.** *Thorax.* 1960, Sept., v. 15, No. 3, 240-43. [25 refs.]

Observations are reported on 100 cases of bronchial carcinoma seen at a thoracic unit in a rural area of Scotland during a 6-year period.

It was estimated that the unit was consulted for about 65% of all patients certified as dying from bronchial carcinoma in the area, and the present series relates to all those in whom the diagnosis was established by bronchoscopy. The area contained no heavy industries and atmospheric pollution was "negligible or very low". No special features were detected to distinguish this

rural series from other series reported from urban areas: sex and age distribution of the patients were the same, no occupation was obviously associated with a high incidence of the disease, the distribution of histological types was normal and the relationship between smoking and bronchial carcinoma appeared to hold as strongly as in other series.

Richard Doll

HOLLAND, R. H., ACEVEDO, A. R. & CLARK, D. A. **The Arsenic Content of Bronchial Mucosa and Submucosa in Man. A Comparison of Specimens from Lung Cancer Victims and Control Tissue.** *Brit. J. Cancer.* 1960, June, v. 14, No. 2, 169-72, 1 fig. [17 refs.]

There is evidence to suggest that populations specifically exposed to arsenic dusts and fumes have an abnormally high incidence of lung cancer [this *Bulletin*, 1958, v. 33, 44]. Since small amounts of arsenic are commonly inhaled in cigarette smoke and in urban air, it is reasonable to inquire whether arsenic deposited in the respiratory system might be a cause of some of the lung cancer now common in many parts of the world. In the present study the arsenic content of the mucosa and submucosa stripped from the main bronchi of 38 subjects at autopsy was measured. In 15 men with lung cancer the results showed that the arsenic content varied from 1.3 $\mu\text{gm.}$ of As_2O_3 per gm. of tissue to 17.9 $\mu\text{gm.}$ with a mean of 7.14 $\mu\text{gm.}$ Specimens from 23 men who had died from other diseases showed a range of 0.75 to 11.1 $\mu\text{gm.}$ per gm. of tissue with a mean of 4.13 $\mu\text{gm.}$ The age distribution at death of the two groups of subjects was similar and there was no obvious difference between their occupations which could account for the different content of arsenic. Lung cancer subjects were much heavier cigarette smokers than the control subjects.

Richard Doll

ROEGHOLT, M. N. Roken en longkanker. [Smoking and Cancer of the Lung] *Nederl. Tijdschr. v. Geneesk.* 1960, Oct. 22, v. 104, No. 43, 2113-23, 2 figs. [275 refs.] English summary.

The English summary appended to the paper is as follows:—

"The author demonstrates that the average consumption of tobacco per smoker has fallen, yet the death rate from pulmonary carcinoma is rising steadily, although not as much as is generally believed. How, then, can there be a causative relationship between these two facts? Medical statisticians of world repute hold that the death rate from pulmonary carcinoma increases with the total amount of tobacco smoked during a lifetime. How does this agree with the author's findings? It can only be explained by assuming that the process is initiated by inhaling tobacco smoke (which was unusual formerly in smoking pipe and cigar) as well as by all factors which change the highly differentiated ciliated epithelium of the lower respiratory passages into pavement epithelium; and that air pollution caused by industry and motorized traffic promotes it. This seems to be the only explanation of this conflicting evidence. The authorities should make

a study of the problem of air pollution and its prevention."

[Quantitative changes in tobacco consumption in Holland are not typical of the changes in other countries, nor is it clear how far the effect of cigarette smoke and of pipe and cigar smoke may depend on differences in the extent to which the smoke is inhaled.]

Richard Doll

CHAPMAN, I. & REDISH, C. H. **Tobacco-Induced Epithelial Proliferation in Human Subject. Long-Term Effects of Pipe Smoking on Epithelium of Hard Palate.** *Arch. Pathology.* 1960, Aug., v. 70, No. 2, 133-40, 5 figs. [11 refs.]

A clinical lesion, characterized by greying and thickening of the mucosa of the hard palate associated with the development of small papules and, in severe cases, with linear retractions and fissuring, is believed to be associated with pipe smoking.

19 elderly male patients were found to show this condition. Their smoking history was recorded and a biopsy taken from the hard palate in 15 of them; a subsequent microscopic examination was made without knowledge of the history. 3 elderly male non-smokers were examined similarly for comparison.

No abnormalities were found in the non-smokers. All the affected patients had been pipe smokers. The severity of the lesion was correlated with the duration of pipe smoking but not with the amount. Examination of the temperature of the smoke at the time it reached the palate, by means of a clinical thermometer strapped to the stem of the pipe, showed that the temperature was only slightly above normal blood temperature. It is suggested that the palatal mucosa of a pipe smoker provides a suitable site for studying the early cytological effects of tobacco smoke on the human epithelium.

Richard Doll

STOCKS, P. & DAVIES, R. I. **Investigation of a Localised High Incidence of Gastric Cancer.** *Public Health.* 1960, Aug., v. 74, No. 11, 408-12, 1 diagram.

Examination of garden soils in North Wales and Cheshire has demonstrated relationships between the amounts of several elements in the soil in the incidence of gastric cancer. The observation that the mortality from gastric cancer was much higher in a small town in Devonshire than in the surrounding area provided an opportunity for seeing whether similar relationships held in another part of the country.

Soil samples were taken from 37 addresses where a death from gastric cancer had occurred in the last 15 years and compared with 72 samples taken from addresses chosen to be representative of the town as a whole. Similar samples were taken from another small town close by where the gastric cancer mortality was low. The levels of organic matter, copper, iron, cobalt, nickel, lead and titanium were all higher in the first township than in the second but there was little difference in the levels of zinc, chromium and vanadium. There was a statistically significant excess of zinc, chromium, cobalt,

nickel, copper, vanadium and organic matter in the soils from addresses where a death from gastric cancer had occurred in both towns compared with control addresses. Excesses of zinc, chromium, cobalt and organic matter had also been found at gastric cancer addresses in North Wales.

Richard Doll

See also p. 124, PAYNE, *The Role of Roasted Chromite Ore in the Production of Cancer*.

See also p. 138, WADDINGTON, *Surgical Aspects of the Mass X-Ray Campaign, Liverpool, 1959*.

DENTAL HEALTH

CANNELL, W. A. *Medical and Dental Aspects of Fluoridation*. pp. vii + 125. [Numerous refs.] 1960. London: H. K. Lewis & Co. Ltd., P.O. Box 66, 136, Gower Street, W.C.1. [15s.]

This is an admirable book in the preface to which the author says "It is hoped that its presentation, in striking a balance between theory and practice, will serve to clarify some aspects of the problem of the prophylactic use of fluoride in dental caries and will further the aims of preventive dentistry in improving public health and well-being".

The chapters are clearly written, have good reference lists and contain much interesting information on the history of fluoridation, influences of nutrition on teeth, influences of civilization on nutrition, fluoride in nutrition, physiology of fluoride and the *materia medica* and pharmacology of fluoride. Separate chapters are on the

calcification of skeletal and dental tissues and on dental enamel, dentine and cementum.

In the final chapter on the public health aspects of fluoridation this subject is well discussed with reference also to the fact that much of the reasoning for or against fluoridation is hampered by lack of information on the possible effects of long-term fluoride administration on human physiology. Further it is stated "The vast amount of dental data derived from ten years' experience in fluoridation in North America has tended to over-emphasise the importance of fluoride in preventive dentistry and to minimise the difficulties of its exploitation on a large scale as a public health measure". Dental caries is not exclusively a dental problem which can be solved by fluoridation alone but with the inclusion of other methods such as change in the dietary habits of the population it will do much to prevent and to control.

There is an appendix on fluoride compounds in industry and a good index.

M. E. Delafield

Sanitation

The order in this section is:—General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

CARLUCCI, A. F. & PRAMER, D. *An Evaluation of Factors affecting the Survival of Escherichia coli in Sea Water*. I. Experimental Procedures. *Applied Microbiol.* Baltimore. 1960, July, v. 8, No. 4, 243-7. [19 refs.] II. Salinity, pH, and Nutrients. *Ibid.*, 247-50. [20 refs.] III. Antibiotics. *Ibid.*, 251-4. [17 refs.] IV. Bacteriophages. *Ibid.*, 254-6. [11 refs.]

I. In the experimental work described in this series of papers a satisfactory medium for the isolation of *Escherichia coli* from sea water was Chapman's Tergitol agar, a culture medium containing proteose peptone 0.5%, Bacto yeast extract 0.3%, lactose 1%, agar 1.5%, "Tergitol 7" 0.01% and bromthymol blue 0.0025%. To this, the authors added 40 p.p.m. of triphenyltetrazolium

chloride sterilized by filtration through sintered glass. On the final medium, *E. coli* gave a brown-centred colony with a yellow halo and *Aerobacter aerogenes* a dark-red centred colony with a blue halo.

Sea water samples were collected 600 ft. offshore in polythene buckets, packed in ice and examined within 1½ hours. Samples examined between June 1956 and June 1958 were of pH 7.8-8 but the salinity fluctuated between 2.7% and 3.2%, being lower after heavy rain. The temperature of the samples at the time of collection ranged from 22°C. in mid-summer down to 3°C. in winter.

When washed *E. coli* cultures were added to sea water, no change in viable counts occurred for 24 hours; there was then a linear fall for 48-72 hours followed by an equilibrium phase. The percentage survival of added

organisms after 48 hours was the index used in assessing the influence of various factors on *E. coli* survival. The authors found that washed cells of pure cultures died out more rapidly in sea water than the coliform bacteria of fresh sewage, the corresponding figures for percentage survival after 48 hours being 7.7 and 53 respectively. Because of this greater sensitivity of pure cultures to adverse influences, these were used in the authors' studies.

No significant differences in percentage survival were found for *E. coli* inocula from cultures incubated between 18 and 24 hours, or with inocula of 10^3 to 10^6 per ml. of sea water. In later work, therefore, a standard inoculum of 10^6 *E. coli* per ml. of sea water, taken from an 18–24-hour culture, was used. As the survival of *E. coli* in sea water was found to vary inversely with temperature, all experiments were done at a standard holding temperature of 28°C.

The authors confirmed that with these methods virtually complete recovery of *E. coli* added to sea water was achieved when samples were taken 1 minute later. Furthermore, when replicate inoculation was done on 3 separate 100 ml. portions of the same freshly collected sample of sea water and survival was determined for 5 days, all counts being replicated 6 times, analysis of variance showed no statistically significant difference between the results obtained from the 3 separate portions. When therefore significant differences were observed in portions of the same sample subjected to different treatments, the differences could be ascribed to the treatment and not to variation inherent in the test procedures.

II. Freshly collected samples of sea water were appropriately diluted with deionized water to give a series containing 0, 25%, 50%, 75% and 100% sea water. These were inoculated with *E. coli* and 48-hour survival levels determined as described above.

The organisms died out more rapidly in deionized water than in 25% sea water, but with higher sea water concentrations the 48-hour survival figures fell rapidly, from 74.5% in 25% sea water to 8.2% in neat sea water. The death-rate of *E. coli* in varying sea water concentrations was found to parallel closely that of the test organism in saline solutions of the same NaCl concentration, as tested in experiments in which sea water evaporated under reduced pressure was re-diluted with deionized water and compared with a parallel series of saline solutions.

The pH range of the sea water samples examined was 7.5 to 8.5. Parallel samples of sea water and of 3% NaCl solution were adjusted to pH values between 5 and 9 and inoculated with *E. coli*. The death-rate was very much more rapid at alkaline pH, 48-hour survival figures for sea water being 58.3% at pH 5 and 0.4% at pH 8.

The influence of organic matter on the survival of *E. coli* in sea water was studied in experiments with sea water to which peptone, glucose or filtered sewage had been added. Glucose had no significant effect on *E. coli* survival. Peptone and filtered sewage favoured survival, and at a peptone concentration of 100 p.p.m. *E. coli* multiplied. In every experiment, however, indigenous sea water bacteria were more favoured than the *E. coli* strain by added nutrients.

III. The possible production by marine bacteria of antibiotics [this *Bulletin*, 1956, v. 31, 856] active against *E. coli* or *Bacillus subtilis* was tested by a replica plate method, but of 200 bacterial colonies from sea water plates tested, none yielded an antibiotic active against these organisms. In further experiments, the authors investigated the stability in sea water of chloramphenicol, chlortetracycline, neomycin, oxytetracycline, penicillin, polymyxin and streptomycin. These antibiotics were diluted to give concentrations of 200 p.p.m. in 500 ml. volumes of untreated and of sterilized sea water, and the samples were stored at 28°C. for 30 days. No loss in antibiotic potency occurred except with chlortetracycline and penicillin, which showed 90% inactivation in 3–4 days and 9 days respectively. This inactivation was apparently chemical and not biological in nature as it occurred equally in raw and sterilized sea water. The viability of *E. coli* was greatly decreased in sea water containing 200 p.p.m. of chloramphenicol, polymyxin and streptomycin but not in concentrations of 50 p.p.m.

IV. The authors had no difficulty in isolating from sea water phages active against *E. coli*. These phages were most stable in autoclaved sea water but rapidly lost their activity in untreated sea water, retaining only 2% of their activity after 10 days' storage. Experiments suggested that coliphage might help in destroying *E. coli* in sea water only if enough organic matter was present to permit prior multiplication of the organisms.

B. Moore

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

ISAAC, P. C. G. & LODGE, Molly. *The Use of Algae for Sewage Treatment in Oxidation Ponds*. *J. & Proc. Inst. Sewage Purification*. 1960, Pt. 4, 376–93, 18 figs. [23 refs.]

This paper was presented at a joint meeting of the North Eastern and Tees and Tyneside Branches of the Institute of Sewage Purification held in Harrogate in March 1960. It is in 4 sections and concerns only those oxidation "ponds in which algal photosynthesis makes a significant contribution to the oxygen needs of the sewage micro-organisms".

The first 2 sections are a review of the operation and design of oxidation ponds under the headings of algal-bacterial "symbiosis", the algal flora of uncontrolled oxidation ponds and algae-bacterial symbiosis in controlled ponds. In California large oxidation ponds are now in use which operate successfully under a wide variety of conditions. "There are at least three valid criteria for assessing the effectiveness of this symbiotic oxidation: the algal yield, the efficiency of energy absorption, and the reduction of B.O.D."

The third section describes an investigation into the effect of certain blue-green (Myxophyceae) algae which

was "undertaken with particular reference to the health needs of the tropics", for the basic "public health" need of "the great majority of tropical countries is more food, especially protein". And this protein may be derived from the synthesis of algal protein while the algae are also breaking down organic wastes. The algae chosen for study were *Anabaena cylindrica*, *Anabaena variabilis*, *Phormidium faveolarum* and *Calothrix membranacea* which are plentiful in tropical habitats. There is a full account of the experiments and of the results obtained. Among the conclusions it is stated that these algae exerted an appreciable effect on bacterial metabolism,

leading to greater purification of the sewage as compared with sewage not so inoculated. BOD reductions of up to 82% were noted over a 12-day period. In a comparison of these results with those obtained with green algae it was found that these grow more quickly than the blue-green algae but that the latter "have the advantage that a higher-quality product is available for future use, if they can be recovered".

The fourth section is on the recovery of algae and the methods of flocculation, ion-exchange and centrifuging investigated in the University of California.

M. E. Delafield

ATMOSPHERIC POLLUTION

DOHAN, F. C. & TAYLOR, E. W. **Air Pollution and Respiratory Disease. A Preliminary Report.** *Amer. J. Med. Sci.* 1960, Sept., v. 240, No. 3, 337-9, 1 fig.

The authors report high correlation coefficients between the incidence of respiratory diseases among women in electronic factories in five U.S. cities and the annual mean concentration of particulate sulphates in the air. There is little or no correlation with other pollutants, and environmental and social factors did not explain the differences in morbidity. The authors attribute these differences to pollution by sulphur dioxide, sulphurous and sulphuric acids and their derivatives.

J. McK. Ellison

WAYNE, L. G. & ORCUTT, J. A. **The Relative Potentials of Common Organic Solvents as Precursors of Eye-Irritants in Urban Atmospheres.** *J. Occup. Med.* Chicago. 1960, Aug., v. 2, No. 8, 383-8, 1 fig.

This screening study was designed to find out how the eye-irritation potentials of certain solvents compared with those of hydrocarbons found in automobile fuels and exhaust gases. Eye irritation in the Los Angeles Basin has been largely attributed to the effects of photochemically induced reaction of oxides of nitrogen with such hydrocarbons. Air containing 20 p.p.m. or 5 p.p.m. of the test vapour and 1 p.p.m. NO_2 was irradiated by Hg vapour lamps or sunlight. An eye-irritation index was calculated for each substance from the periods, up to 90 seconds, until panels of 8-11 persons detected irritation

when, by means of a fitted eye-piece adaptor, the eye was exposed to the warm irradiated atmosphere. Indices are given for 6 hydrocarbon fractions of various boiling points; 11 solvents; 4 pure hydrocarbons for comparison and, for 5 of the solvents, which gave high values with artificial light, control values with no light irradiation. Indices of the hydrocarbon-fractions did not correlate with boiling points.

Among the solvents, none showed eye-irritation potentials appreciably greater than those shown by 2 pure olefines. Most showed potentials at least as great as that of n-hexane, which was relatively unreactive. Though the average effect of the 4-fold reduction in concentration increased the panel response time by about 40%, ranking in order of potency was essentially the same at both concentrations for 8 solvents.

The problems of applying such data to the estimation of the effects of atmospheric contamination under smog conditions are discussed. However, the assumption that the relative potentials observed in the experiments would apply at atmospheric concentrations leads to an estimate that the contribution which is possible by solvent vapours in Los Angeles is about one-tenth of that caused by exhaust and petrol vapours.

M. Patricia Fitzsimons

SCHULZ, E. J., DUFFEE, R. A., MITCHELL, R. I. & UNGAR, E. W. **A Tracer Technique to Measure Deposition of Stack Emissions.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 343-9, 5 figs.

MAGA, J. A. **Statewide Air Pollution Standards in California.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 430-35.

Occupational Hygiene

The order in this section is:—General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.

GENERAL

MEIKLEJOHN, A. **Occupational Health in relation to the Health Services of Great Britain.** *Indust. Med. & Surgery.* Miami. 1960, Sept., v. 29, No. 9, 405–12.

This review of the British Industrial Health Services is intended for the information of doctors in other countries. A proper understanding of our occupational health practice cannot be obtained, however, without an intimate knowledge of the general health services, and a description of the National Health Service is given as a background.

The occupational health services are of two types, statutory and voluntary. The statutory services include the Factory Inspectorate, the Appointed Factory Doctors, and the Inspectorate of Mines. One of the points made is that the Factory Inspectorate may seem to pay too much attention to industrial poisoning and diseases, but the low incidence of these conditions is due to the effectiveness of preventive measures of supervision.

The voluntary services are maintained by the employer. They vary greatly in their scope and depend largely on the size and prosperity of the firm, the outlook of management, nature of work and production and specific hazards.

Overseas readers will find this an excellent and concise account of our industrial services. They may, perhaps, not be as interested as readers at home in the details given of the limitations and defects. For example the duties of the Factory Inspectorate are limited to factories and do not extend to shops, offices, transport and agriculture. The number of inspectors is small and they lack certain facilities. Only minimum standards can be enforced. The voluntary services are mostly confined to the large factories. In small firms up to 50 workers, services are almost non-existent, and in many the working conditions are bad.

The times are favourable for a change. All political parties support the idea of an Occupational Health Service into which the existing good but fragmentary services can be incorporated. There is danger, Meiklejohn says, in that too much exploration may result in too little and too late action. *Charles L. Sutherland*

MUNARI, Maddelena & TINAZZI, V. Indagini clinico-statistiche su 348 autisti abilitati alla patente di terzo grado. [A Clinical and Statistical Survey of 348 Drivers holding "Grade III" (Commercial) Driving Permits] *Rass. Med. Indust.* Turin. 1960, Mar.–Apr., v. 29, No. 2, 145–57. [22 refs.] English summary.

An investigation carried out in Italy into 167,574 road accidents during 1956 showed 135,354 to have been due to the human factor—a proportion of 81%. Failure to

comply with the highway requirements accounted for 78,424, carelessness for 54,018 and abnormalities of either a physical or a psychological nature for the remaining 2,912.

The authors base the present report on the results of medical examination which they have carried out for the purposes of industrial insurance on 348 holders of a "Third Degree"—commercial—driving licence. Their ages ranged from 20 to 64 years, and their driving experience from a few months to 26 years. The transport undertaking required this examination when 304 of these subjects were offering themselves for engagement, while the other 44 were being subjected to the medical examination when already in the service: judgment and action on the findings necessarily differed in the 2 groups. The nervous, psychiatric, respiratory, circulatory and digestive systems, eyesight and hearing were investigated in each case and the findings are summarized in tabular form. 39 were considered to be unfit to hold the licence. 80 other subjects showed psychological or physical defects which disqualified them for engagement by the undertaking though they complied with the requirements which the existing law laid down for holding a "Third Degree" driving licence. The authors consider that the law should be tightened up in the interest of reducing the incidence of road accidents. *J. Cauchi*

BONATI, G. Sordità professionale da rumore in talune categorie di operai dei cantieri navali. (Casistica clinica.) [Professional Deafness, caused by Noise, of Some Categories of Workmen in Shipyards] *Rass. Med. Indust.* Turin. 1960, Mar.–Apr., v. 29, No. 2, 127–44, 3 figs. [10 refs.] English summary.

A new Italian law has made provision, since 1952, for the payment of industrial compensation in 40 occupational diseases, instead of 8 as previously: the additions include occupational deafness. The figures accepted as the limits within which is the threshold at which noise begins to injure the sense of hearing range from 80 to 100 decibels.

The author has studied deafness from noise in the employees of a shipyard. Repeated trauma from noise induces at first a defence mechanism in the middle ear, where the muscles of the ossicles take up a more rigid position, while the sensory elements of the inner ear acquire a degree of resistance to the noise stimuli: it is all part of the process of adaptation to the noisy environment. Very gradually the affected workman becomes aware that his hearing is diminishing.

The experience which the author here reports on covers 2 years' medical care of 103 employees of a large shipyard. 36 riveters, who work in pairs, and 33 caulkers

were exposed to noise from pneumatic hammers and mechanical drills and chisels; resonance from the empty hull aboard which they worked intensified the noise. These workmen were subjected to continuous noises of the order of about 105 decibels as well as to intermittent noises of some 120–140 decibels. In the fitting and testing of internal combustion (diesel) engines and of turbines, 34 motor mechanics were employed, and exposed to noises of the order of 90–100 decibels, which are of a low-pitched quality and more or less continuous. The ages were 31–60 and seniority at the job was in no case less than 10 years, in some over 30. The loss of hearing was recorded as a percentage and affected every single riveter and caulker, while 11 or 32% of the motor mechanics escaped.

The author prescribed selective ear plugs, equipment to cushion the vibrations between tool and handler and appropriate periods of rest with good results.

J. Cauchi

BOSSO, G. C. & PACCAGNINO, F. Sulle lesioni corneali dei lavoratori agricoli della provincia di Novara. [Corneal Lesions in Agricultural Workers of the Province of Novara] *Med. d. Lavoro*. 1960, May, v. 51, No. 5, 381–4. English summary (6 lines).

The authors have investigated the corneal lesions suffered by agricultural workers, mostly on rice cultivation, in the Province of Novara in the 5-year period 1955–59. There were 148 cases in men and 96 in women, though the latter form the majority of the rice workers. The initial trauma is believed to be from the sharp end of a grain of rice or wheat and the injury is sustained when either carrying the sheaves or bending over the crop during various operations. Infection of the corneal wound supervenes and the process is aggravated if there are pre-existing conditions such as dacryocystitis, obstruction of the tear passages, ectropion or previous conjunctivitis. Perforation of the cornea, a descemetocoele or other serious complications may develop.

The occupational complaints which this paper deals with prevail in summer (May–August), in the busy season when immigrant workers join the local farm labourers. All those at risk should be educated to the importance of seeking the earliest possible treatment for any eye complaint no matter how trivial. Protective goggles can be worn with advantage. Pre-existing abnormalities of the cornea and of the lachrymal passages should be looked for and treated.

The corneal condition has been cured with antibiotics, applied locally or injected subconjunctivally or parenterally according to the severity of the case. Cauterization with tincture of iodine or mercurochrome proved useful in some. Pressure may have to be relieved by tapping the anterior chamber.

J. Cauchi

MISKOLCZY, W. Malzfieber. [Fever in Workers in Malt] *Zent. f. Arbeitsmed. u. Arbeitsschutz*. 1960, Aug., v. 10, No. 8, 184–9.

The investigation here described was undertaken because workers with malt in a brewery complained of

attacks of fever with catarrhal symptoms. There is a detailed account of the production of malt from barley and of the enzymic actions which occur, after which the malt is dried and ground with the formation of a considerable amount of dust. In this brewery, maize, molasses and rice are additions in the manufacture of beer.

A large number of examinations were carried out at different points in the brewery to determine the number and size of the malt dust particles in the atmosphere. Bacteriological investigations of the dust were also carried out. The findings of these examinations yielded no explanation of the causation of the feverish attacks and it is considered therefore that the cause must lie in the chemical structure of the seeds from which the malt is prepared. Extracts were made from 3 different kinds of malt and used in intracutaneous skin tests of a number of malt workers and control workers. All the malt workers but only 1 of the controls gave a positive skin reaction. It is concluded that there is some allergic substance in the malt and its dust which plays a part in the causation of the feverish illness of the malt workers.

The workers state that after 2 or 3 hours they begin to cough. In the evening the body temperature rises to 37.3° to 37.8°C. but by the next morning it is normal. X-ray shows increase in transparency and size of the hilum. Vital capacity was found to be reduced in all the men.

M. E. Delafield

GOLDMAN, E. I. [Problems of Industrial Hygiene in the Manufacture of Crystalline Transistors] *Gigiena Truda i Professional'nye Zabolevaniya*. Moscow. 1960, v. 4, No. 10, 30–35. [In Russian.]

The English summary appended to the paper is as follows:—

“In the manufacture of high-frequency transistors factors are encountered capable of producing unfavourable effect on the health of the workers. They include: pollution of the air medium with various chemical substances, their hydrogenous and other compounds (germanium, antimony, arsenic, plumbum, etc), formation of dust, which carries the above elements, their alloys, silica and other compounds; contamination of the surrounding air with the vapours of solvents, acids, alkali and organic compounds.

“At the sections of the plant, where germanium and silicon undergo alloyage, operators may become subject to the influence of electromagnetic fields, while in the control sections—to those of ultra-high frequency and soft X-ray radiation. The manufacturing process implies many fine operations associated with a considerable strain on the eyes.

“Hygienic improvement of the work conditions in the manufacture of high-frequency transistors should follow the lines of maximal mechanization of industrial processes, localization and disposal of developing vapours, gases and dust. It should also provide for the protection against electro-magnetic fields, ultra-high frequency fields and soft X-ray radiation, for effective illumination in operations involving fine visual work and, finally, secure adequate means of individual protection to all of the operators.”

OCCUPATIONAL DISEASES

McINTYRE RESEARCH FOUNDATION. **Conference on Silicosis and other Industrial Pulmonary Diseases 1960.** *Indust. Med. & Surgery.* Miami. 1960, June, v. 29, No. 6, 231-304, numerous figs. [Numerous refs.]

The McIntyre Research Foundation on Silicosis originated 25 years ago in the mining industry in the Province of Ontario, Canada. The founders' objective was the mitigation of silicosis as an industrial disease. During the past 11 years the Foundation has held 10 conferences. J. W. G. HANNON, Medical Director of the McIntyre Research Foundation, Washington, Pa., and conference chairman, states in an introductory note that "because of the outstanding quality of the papers presented at the 1960 Conference it was agreed to have all the papers published by *Industrial Medicine and Surgery*. In this manner the McIntyre Research Foundation could share their new scientific information with the many readers of this Journal".

Twelve papers were presented, covering practically every clinical and scientific aspect of occupational diseases of the lungs. The emphasis was on experience of silicosis in metalliferous mines in North America. With the exception of Professor J. GOUGH, Cardiff, the contributors, medical and non-medical, were from Canada and U.S.A.

K. E. ROBINSON. *A practical method of providing a suitable in-plant environment* (pp. 233-237).

Comfort at work is usually considered to be attained when the heat gain and loss of the body are so regulated that the workman is not conscious of heat or cold. The author discusses the basic facts about wet and dry bulb thermometer readings, air movement, effective temperature and radiant and convected heat. The engineer's responsibility is "one of controlling the workman's rate of heat loss, not, as is often stated, of heating him". In an enquiry in U.S.A. most workmen favoured an effective temperature of 71°F. for summer and 68°F. for winter. Various systems of in-plant ventilation are discussed. Particular attention is directed to industrial operations which require additional exhaust to control dust and fumes in the atmosphere. Exhausting of large quantities of air results in high infiltration rates at all doors, windows and other openings.

[This is a well presented practical paper, with excellent diagrams.]

P. A. THEODOS. *The clinical significance of cavitation in anthracosilicosis* (pp. 238-242).

Over a period of 12 years, 1,847 hard-coal miners from the anthracite regions of Pennsylvania were studied at the Barton Memorial Division of the Jefferson Medical College Hospital, Philadelphia, Pa. All were suffering from anthracosilicosis. Each case was investigated radiographically, including planigrams (tomograms). Sputum studies for acid-fast bacilli were very intensive and included direct smear, 24 and 48 hour concentrates,

culture and examination of fasting gastric contents. Cavitation was observed in 191 (10.3%) cases.

Cavitation in Silicotic Miners by Cause

	Number	%
Tuberculosis	139	72.8
Ischaemic Necrosis	44	23.0
Broncogenic Carcinoma	2	1.0
Cystic Bronchiectasis	2	1.0
Undetermined	4	2.2
Total	191	100.0

Dr. Theodos comments that: "Recognition of the non-tuberculous nature of cavitation is important so that unnecessary hospitalization in a tuberculous facility can be avoided and the use of IPPB [intermittent positive pressure breathing] is not withheld."

[The findings recorded are similar to those of other observers. The scheme for discovery of acid-fast bacilli is of great interest. The small radiographs used for illustration are very good, but the dating of films in figure 6 in the American fashion, namely 12.18.57 and 1.21.58, may be confusing to British readers.]

H. S. VAN ORDSTRAND. *Diffuse lung lesions that mimic pneumoconiosis* (pp. 243-246).

The title of this paper fully represents its theme. The author underlines that non-occupational lung diseases occur in workers in dusty trades and so there is a need for physicians and radiologists to be alert to this possibility and not routinely to attribute the disease to dust.

[In the differential diagnosis of pneumoconiosis the need is to maintain perspective and never to forget that the radiograph is only part of the evidence. Not unnaturally in the case of lung disease in a workman who is or has been employed for a substantial period in a recognized dust hazard, one almost immediately thinks of pneumoconiosis. The crucial point is to discover anomalous features and to explore these fully. If this is done thoroughly few wrong diagnoses will result. *Experientia docet.*]

W. TAYLOR. *The value of large lung sections in the study of diseases of the chest* (pp. 247-250).

The study of large lung sections is valuable in teaching, in the correlation of findings in life and at autopsy and in the determination of compensation claims. A detailed account is given of the Blanchard modification of the Gough Technique.

[In addition to the uses mentioned, large sections by their convenient form have become indispensable items in the complete dossier of individual cases. As a large number can be prepared it is possible to build up collections of particular appearances (see later Gough on centrilobular emphysema) and finally they can be exchanged between workers throughout the world. Professor Gough and his colleagues at the Welsh National School of Medicine, Cardiff, merit the gratitude of all for the generosity with which they have distributed specimens now for many years.]

A. D. CAMPBELL. *Johannesburg Pneumoconiosis Conference* (pp. 251-259).

In February, 1959, the South African Council for Scientific and Industrial Research under the direction of Dr. A. J. ORENSTEIN convened at Johannesburg a conference of experts on pneumoconiosis. Dr. A. Campbell attended and this paper is a comprehensive report of the proceedings and recommendations.

[J. and A. Churchill Ltd., London, published in September 1960, the complete papers entitled *An International Symposium on Pneumoconiosis*, edited by A. J. Orenstein.]

E. O. T. SIMPSON. *Problems of silicosis in British Columbia* (pp. 260-264).

British Columbia is one of the oldest mining provinces in Canada. Its mines have been active for more than 100 years. Silicosis was not made compensable in the province until 1936, although the disease had been made compensable in Ontario 10 years previously.

Compensation payments are a heavy burden particularly in times of depression. It is argued that mining companies today are compelled to accept responsibility for the sins and omissions of past generations and concurrently to ensure that future generations may benefit from good mining practices and preventive measures. The plea is that the provincial government directly and through reciprocal arrangements with other provinces should afford some financial relief to existing companies.

[The arguments are very familiar. It is a sad reflection that in most countries the financial screw has been necessary to encourage preventive measures.]

W. C. WHEELER & A. H. SELLERS. *Recent trends in silicosis among miners in Ontario* (pp. 265-272).

Silicosis was designated as an industrial disease for compensation purposes in the Province of Ontario in 1926. In 1950 a Medical Statistics Unit was set up under the Workmen's Compensation Board to prepare and analyse data on the incidence, prevalence and progression of silicosis in the mining industry in Ontario. The trends to date are described and illustrated by tables, graphs and histograms. The X-ray findings are classified on a 9-point scale, in which 5—"generalized arborization with partial mottling" is the first definite sign of silicosis. The authors suggest that this Medical Statistics Unit would be a valuable aid to a Pneumoconiosis Research Unit if such were to be established in Ontario.

A. H. SELLERS. *Mortality from occupational diseases of the lung in Ontario* (pp. 273-277).

The content of this contribution may be represented by the following excerpt:

"Of the 251 men compensated for occupational disease of the lung (silicotics) dying in Ontario during the five years 1954-58, occupational disease of lung, with or without tuberculosis was mentioned in 205 or 81.7%. In 136 or 54.2% of the total, death was attributed to occupational disease of the lung, 41 with and 95 without mention of tuberculosis. In the 69 [this is 33.6% of the 205 deaths mentioned above] others in which occupational disease of the lung was mentioned on the medical certificate or 27.5% of the total of 251 (14 with and 55 without mention

of tuberculosis) death was assigned to other causes. Of the 14 with mention of silicosis and tuberculosis that were attributed to other causes, 6 were assigned to cancer and 7 to arteriosclerotic heart disease or cerebral embolism.

"In 46 cases or 18.3% of the total, there was no mention of tuberculosis or occupational disease of lung (silicosis or other pneumoconiosis) on the medical certificate of death. In these 46 cases death was attributed to a variety of causes; cancer, seven; cerebral haemorrhage, embolism and thrombosis, seven; cardiovascular disease, 20; injuries, three; and other conditions, nine."

Future studies are intended to refine the available information.

[The data presented have considerable interest as statistics. Future reports would be enhanced by some discussion of certification of the cause of death in cases of pneumoconiosis associated with extraneous disease.]

G. GRASSMÜCK. *The dust control and ventilation services of the Quebec Metal Mines Accident Prevention Association* (pp. 278-282).

The purpose of this unit is to advise and assist the members of the Association in the technical and organizational means of maintaining and improving dust control and ventilation, both underground and in surface plants. At present the services are at the disposal of 37 mines of which 13 are gold mines, 19 base and other non-ferrous metal mines and 5 iron mines. There are no producing uranium mines or coalmines in Quebec, the territory covered by the scheme. The McIntyre Aluminium Powder Prophylaxis is being applied at present at 12 Quebec metal mines.

J. GOUGH. *Emphysema in relation to occupation* (pp. 283-285).

Emphysema is defined as a condition of the lung characterized by increase beyond the normal in the size of air spaces distal to the terminal bronchiole either from dilation or from destruction of their walls.

The Ciba Guest Symposium [this *Bulletin*, 1960, v. 35, 419] proposed a classification based on morbid anatomy. Two alternatives to this classification are suggested; the ingredients are the same in both but in the one the primary distinction is the anatomical distribution, whereas in the other it is the presence or absence of destruction. These classifications are set out in detail.

Professor Gough discussed focal emphysema, emphysema in silicosis, emphysema due to cadmium and centrilobular emphysema.

Focal Emphysema

A uniform distribution in the lung is usual.

Nondestructive

(fusiform dilatation of respiratory bronchioles).

Dust sheathing of the spaces.

No inflammatory changes in the bronchiolar pathways.

Normal airway calibre.

Centrilobular Emphysema

Often patchy and may be quite localized.

Destructive

(disintegration of distal respiratory bronchiole).

Only normal quantities of dust.

Bronchiolitis and inflammatory change within the parts of the lesion itself.

Normal, dilated or narrow airways.

Readers who are concerned with the aetiology of bronchitis in dusty occupations and its significance in

relation to compensation for pneumoconiosis may be interested in these quotations:

"There is an important relationship between the presence of bronchitis and the accumulation of dust in the lungs. The relationship is an inverse one, that is to say if there is chronic bronchitis, less dust will be accumulated in the lungs. This is presumably due to the dust being swept out in the increased secretions."

"If as is usually the case, the payment of compensation requires radiological evidence of dust disease, those with chronic bronchitis and normal chest radiographs may feel unjustly treated."

J. W. G. HANNON, P. G. BOVARD & L. R. OSMOND.
Roentgen study of silicosis in ceramic workers who have received McIntyre aluminium powder (pp. 286-289).

Silicosis is a recognised risk of certain occupations in the pottery industry. At a factory engaged in the manufacture of sanitary earthenware it was observed that dust control, medical control and educational programmes were not able to eradicate the silicosis hazard. 132 sanitary casters were treated once weekly by inhalations of McIntyre aluminium powder. The authors believed that the development and progression of silicosis could be measured by the use of X-ray films. [There were no controls.] The conclusions were:

(1) The inhalation of McIntyre aluminium powder can help protect the workers from silicosis over 15+ period of years.

(2) The use of McIntyre aluminium powder will prevent or decrease the rate of severity of the usual progression of ceramic silicosis.

(3) There was no evidence that the inhalation of McIntyre aluminium powder was harmful in any manner to the workmen who took this type of additive prophylaxis in the prevention of silicosis.

[This does not accord with English experience among pottery workers (see this *Bulletin*, 1956, v. 31, 1018).]

G. R. MENEELY. *Practical evaluation of the function of the lungs* (pp. 291-304).

This contribution, within the limits of space, is an excellent exposition of the physiology of respiration and its measurement in health and disease, actual or alleged. The illustrations are clear and informative. Among the interesting comments by the author are these:

"Pulmonary function tests cannot supplant a careful history, physical examination, and fluoroscopic and radiological examination, nor can they supplant bacteriological or pathological studies. It is important to emphasize that no single test now known is sufficient for evaluation of all aspects of pulmonary function nor is there any single test which can be relied upon absolutely as a screening procedure to identify those patients in whom further studies ought to be done."

"They certainly should be used in pre-employment evaluation. Pulmonary function tests are valuable as *an aid* [italics inserted] in evaluating disability claims in insurance or industrial practice." A. Meiklejohn

SCHEPERS, G. W. H. *Theories of the Causes of Silicosis. Parts I, II & III.* (Presented at the McIntyre Research Foundation Conference on Silicosis and other Industrial Pulmonary Diseases, January 25-27, 1960, Toronto, Canada.) *Indust. Med. & Surgery*. Miami. 1960, July, Aug. & Sept., v. 29, Nos. 7, 8 & 9, 326-33; 359-69; 434-39, 30 figs. [Numerous refs.]

[Dr. W. H. Schepers is a recognised international authority on the pneumoconioses. Originally he was a member of the Silicosis Medical Bureau in South Africa. Thereafter he worked at the Saranac Laboratory in U.S.A. in association with Professor A. VORWALD. He is now research director at the Haskell Laboratory for Toxicology at Wilmington, Delaware, U.S.A. During the past 10 years he has made outstanding contributions to the experimental study of the pathogenesis of many varieties of pneumoconiosis.]

In this paper his aim is to survey comprehensively and critically the various theories which have been advanced at different periods to explain the causation of silicosis. The concepts are considered under the broad headings, exploratory, chemical, physical and biological. The period covered is from 300 B.C. to 1960. The 4 groups are set out in separate tables under the headings, theory, author and date. Finally Dr. Schepers attempts a synthesis of available information.

[This survey is highly commended to readers not only for the broad general statement of the subject but for the critical evaluation of the various theories. It provides an excellent introduction to the present biological concepts. Readers will observe a few errors in the citations but these do not diminish the value of this encyclopaedic essay.]

[See MCINTYRE RESEARCH FOUNDATION, p. 115.]

A. Meiklejohn

HOUBERECHTS, A. *L'activité de l'Institut d'Hygiène des Mines au cours de l'année 1959. [The Work of the Institut d'Hygiène des Mines during 1959]* Reprinted from *Ann. Mines Belgique*. 1960, No. 5, 43 pp., 29 figs. [70 refs.]

Since 1948 the annual report on the work of the Institute, which is under the distinguished direction of Professor A. Houberechts, has been included in the *Annales des Mines de Belgique*. It has been distributed privately as a reprint. The majority of communications on the research work and analyses of medical and technical literature have been issued as separate bulletins multi-graphed for distribution. These publications have been highly commended and are increasingly in demand. Accordingly the Council of the Institute decided that after 1960 they will publish a quarterly journal entitled *Revue de l'Institut d'Hygiène des Mines*. This will replace the bulletins and will be available to subscribers.

The present report follows those of previous years. It is divided into 2 sections, medical and technical (mining engineering).

During 1959 in addition to routine medical examinations of miners at the Institute and at the collieries (mobile unit) the programme of research continued. The subjects investigated included measurements of pulmonary function, a study of various aspects of pulmonary circulation in pneumoconiosis, with radio-active iodine 131 as a tracer, and the topographical distribution of massive fibrosis in pneumoconiotic lungs [this *Bulletin*, 1960, v. 35, 110]. As in previous years the technical experts have been mainly concerned with dust measurements and the human engineering problems of work underground at high temperatures.

[A notable feature of this and previous reports is the excellent list of references. These are listed numerically. In welcoming the proposed new journal I would respectfully suggest that the editors should adopt the Harvard system.]

A. Meiklejohn

WESTERBOER, I. Zur Routinemessung der Korngrößenverteilung von Feinstaub-Niederschlägen im Thermalpräzipitator mit Hilfe des Elektronenmikroskopes. [On the Routine Measurement of the Size Distribution of Thermal Precipitator Samples by Electron Microscopy] *Staub*. Düsseldorf. 1960, Oct. 1, v. 20, No. 10, 361-4, 2 figs. [11 refs.]

It is customary to count and size dust particles over the whole width of a thermal precipitator deposit because the size distribution across the deposit varies. The object of the present paper is to see whether a single field in the centre of the strip can be found which would have the same size distribution as the whole sample.

It was found that no such field exists with thermal precipitators which use heated wires but with Walkenhorst's modification of the thermal precipitator [this *Bulletin*, 1956, v. 31, 44] in which a flat platinum strip of 1.5 mm. width is used as heating element, the centre of the deposit was found to show a size distribution of dust (with two test dusts) very similar to that of the average taken over the whole dust trace. Details of the technique used by the author are given and discussed in comparison with similar methods found in the literature.

G. Nagelschmidt

SCHMIDT, K. G. Die Routinebestimmung von freier Kieselsäure im Phosphorsäureaufschluss. [Routine Estimation of Free Silicic Acid by Means of Phosphoric Acid Decomposition] *Staub*. Düsseldorf. 1960, Nov. 1, v. 20, No. 11, 404-11, 6 figs. [11 refs.]

The English summary appended to the paper is as follows:—

"The *Staubforschungsinstitut* method for the determination of free silicic acid using phosphoric acid decomposition is described and discussed. At present there is no more accurate method available for the determination of free silicic acid in rock and earth substances. For combustion products X-ray analysis may be superior. Some substances, such as SiC and fluorine containing substances are better determined by optical means."

YUSA, T. [Studies on the Normal Standard of Ventilatory Function in Muscular Labourers] *J. Sci. of Labour*. Tokyo. 1960, Aug., v. 36, No. 8, 427-31, 4 figs. [11 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"As most silicotic patients in this country are muscular workers such as miners and stonecutters, whose ventilatory functions are usually highly developed, it seems to be important to use an adequate normal standard for muscular workers in estimating their ventilatory insufficiency, for this reason, determinations of vital capacity, maximum breathing capacity and timed vital capacity of 312 healthy muscular workers were made by 13.51 respirometer of Benedict-Roth type, to obtain the normal standard in ventilatory function.

"1. There was found no significant difference between the average vital capacity of the muscular workers and the standard presented by Ebina. The latter seems to be useful in evaluating the vital capacity of muscular workers and silicotic patients.

"2. Regarding the maximum breathing capacity, the muscular workers showed a markedly higher value compared with the standard presented by Motley using 13.51 respirometer of Benedict-Roth type.

"3. There was found no significant difference between the average timed vital capacity of the muscular workers and the standard value presented by Nakamura.

"4. According to the results of the author's determinations, the normal level of ventilatory function in muscular workers can be predicted by the following formulas:

"Vital Capacity (cc)=[27.48-0.169 (Age-20)] × Height (cm).

Maximum Breathing Capacity (1 min.)=[113.5-0.686 × Age] × Body Surface Area (m²).

Timed Vital Capacity (cc/sec.)=[2.29-0.0202 × Age-20] × Body Surface Area."

PERRET, C. La mécanique respiratoire dans la fibrose pulmonaire. [The Mechanics of Respiration in Pulmonary Fibrosis] *Schweiz. med. Woch.* 1960, Oct. 8, v. 90, No. 41, 1129-36, 4 figs. [51 refs.]

[The study of the mechanics of respiration has given fresh impetus to the investigation and assessment of chronic pulmonary diseases. It provides a valuable supplement to the information derived from measurements of pulmonary ventilation and gas exchange between the lungs and the blood.]

After a careful review of the relevant literature, the author, Dr. C. Perret of the University Medical Clinic at Lausanne, describes an investigation into pulmonary compliance which he made in 9 cases of chronic pulmonary fibrosis; diffuse interstitial fibrosis 1 case; scleroderma and sarcoidosis, each 2 cases; asbestosis 1 case; and 3 cases of undetermined cause.

The method consisted of intrathoracic pressure recordings by means of an oesophageal balloon with direct recording of the volume/pressure tracing on photographic paper. In addition the standard measurements of pulmonary ventilation and gas exchange were made.

In all 9 cases compliance was less than normal as compared with a control group of 16 healthy subjects. Compliance varied directly with vital capacity and was lower during muscular exercise than at rest.

This reduction of pulmonary compliance was observed even in the first stages of the disease, when the usual functional tests (spirometry, respiratory exchange and arterial blood gas tensions) do not show any alteration.

"The reduction of the compliance has for its corollary an augmentation of respiratory work by increase of elastic work. This augmentation is clearly shown if the work is expressed as a function of the oxygen consumption, measured in steady state. This parameter that we call 'mechanical equivalent for O_2 ' is expressed in kgm. per litre of oxygen consumed.

"The elevated respiratory frequency and the much reduced tidal volume observed in these patients are interpreted as a phenomenon of adaptation to the mechanical conditions, permitting these patients to diminish as much as possible the work spent against the increased resistance to lung expansion."

The author concludes that the determination of dynamic pulmonary compliance affords a useful method of assessment in cases of chronic pulmonary fibrosis. It is particularly valuable in those cases in which clinical, radiological and usual functional tests fail to account for the dyspnoea and alleged diminished capacity for work.

A. Meiklejohn

BÜHLMANN, A. & SCHUPPLI, M. Atemmechanische Untersuchungen bei Silikose. [Mechanics of breathing in Persons with Silicosis] *Deut. med. Woch.* 1960, Sept. 30, v. 85, No. 40, 1745-50, 1782-3, 3 figs.

Up to now, according to the authors, no reports of systematic investigations into the mechanics of breathing in lung fibrosis of the various forms of silicosis have appeared in journals using the German language. The present report covers only silicosis cases, 35 in number, 2 of these were of the "subacute" type, a rapidly progressing form of fibrosis leading to death in 3 or 4 years from the commencement of exposure in sandblasting. The remainder were "ordinary" cases which either progress slowly or remain stationary over years. These were drawn from miners, dressers of castings, stonemasons and pottery workers. 23 of them were of a severe type judged by the radiograph and 10 were of a milder type. The tests applied included spirometry, 1-second Tiffeneau test, the assessment of blood gases in rest and exercise, oesophageal pressures, and pneumotachograms. In the 2 subacute cases there was a reduction in the lung volume along with a diffusion defect for oxygen; the CO_2 tension was about normal, showing that the ventilation was quantitatively adequate. The lung expansion was reduced and the elastic resistance raised. The viscous resistance on the other hand was about normal. These changes correspond to those found in diffuse fibrosis such as asbestosis, the HAMMAN-RICH syndrome etc.

In the ordinary type, the lung volume was on the average normal, and where it was altered there was no correlation with the severity of the silicosis as shown by

the radiograph. The elastic resistance was not raised except in one case of severe silicosis, where parts of the lung were overdistended. Viscous resistance was raised in 14 out of the 33 cases owing to flow resistance in the air passages due to bronchial obstruction. The correlation between the 1-second Tiffeneau test and viscous resistance is discussed: it is stated that no patient with a raised viscous resistance has a normal 1-second volume but that conversely some cases with a normal viscous resistance show a relatively poor 1-second volume. Patients with raised viscous resistance show chronic bronchitis on clinical investigation.

The findings of lung function tests in these cases agree with those from patients with chronic bronchitis and obstructive emphysema without silicosis.

Charles L. Sutherland

VORWALD, A. J. Diffuse Fibrogenic Pneumoconiosis. *Indust. Med. & Surgery.* Miami. 1960, Aug., v. 29, No. 8, 353-8, 11 figs.

[This paper was presented at the Conference of the MCINTYRE RESEARCH FOUNDATION on Silicosis and other Pulmonary Diseases, see p. 115.]

The pneumoconioses are usually recognized as belonging to one or the other of two major categories, the biologically inert or the biologically active. The second category may be considered under two headings, one which is defined pathologically by nodular or semi-nodular lesions uniformly scattered throughout the entire lung, and the second characterized by a non-nodular, diffuse and widespread pneumonitis.

This second group of diffuse fibrogenic pneumoconiosis is discussed in this paper. A group of normal rabbits was exposed from 90 to 510 days by inhalation to a silicon dioxide fume which had a mean atmospheric concentration of 1.47 mgm. per cubic foot of air, and which had a particle size of from 0.009 to 0.1 micron in diameter. The rabbits showed a gradual development of respiratory difficulty which became more severe with increasing length of exposure. The most striking observation made during life was that at least two of the animals showed a progressive and pronounced increase in the right ventricular pressure. Pathologically, the lungs were found to have a degree of emphysema proportional to the exposure. The emphysema was fine and diffusely distributed; with longer exposure, however, the emphysema was coarser. On microscopical examination there was a chronic diffuse interstitial inflammation which thickened the alveolar walls with the production of scattered stellate lesions of cellular fibrosis. These experimental findings suggest that excessive quantities of inhaled silica particles of ultramicroscopic size may induce similar changes in human subjects. These may be compared with the results found in workers manufacturing corundum from bauxite, and also in workers engaged in the high temperature calcination processing of diatomaceous earth, in addition to the well-known changes in asbestosis and talcosis.

A male worker who had been exposed to natural and artificial graphite dusts for 10 years was found at death to show extensive indurative fibrosis. Microscopically areas of focal and of diffuse fibrosis were found along

with some massive lesions. Natural graphite contains from 61.7 to 96.2% of graphite, silica from 1.56 to 19.2%. Artificial graphite is almost pure graphite, with only 0.44% of quartz. These forms of graphite were tested by intratracheal injection in a series of rats. Artificial graphite acted only as an inert substance even after a year, while natural graphite provoked a focal and diffuse pneumonitis. The severity of this reaction was proportional to the amount of free silica in the sample tested.

A second case was of a man exposed for 30 years to a dusting powder used in rubber manufacture. At autopsy a widespread diffuse fibrosis along with massive lesions and emphysema was found in the lungs. Crystals were found in the lung which proved on X-ray diffraction analyses to be mica. Under the polarizing microscope the crystals appeared to be long and narrow and had the optical properties of mica but a few might have been talc. No crystalline silica was found. Experiments on rats by the intratracheal route were made with mica; they produced only a mild reaction which had largely disappeared after a year. It was therefore not proved that the mica produced the lesions in the second case. Vorwald says that the problems of diffuse pulmonary fibrosis are in need of continued study.

[There was no record of pulmonary function tests during life in the two cases. The degree of alveolar capillary membrane block would have been of interest.]

Charles L. Sutherland

BYERS, P. D., KING, E. J. & HARRISON, C. V. The Effect of Triton, a Surface Active Polyoxethylene Ether on Experimental Infective Pneumoconiosis. *Brit. J. Exper. Path.* 1960, Oct., v. 41, No. 5, 472-7, 6 figs. on 2 pls. [14 refs.]

The authors have already shown that Triton has no effect on quartz induced silicosis in animals [this *Bulletin*, 1961, v. 36, 24]. In view of the work of REES on the prevention of tuberculosis in mice by Triton [*Ibid.*, 1953, v. 28, 1031], it was thought worth while to determine whether it had any effect on the highly modified form of tuberculosis induced in animals by a mixture of dust with a relatively small number of tubercle bacilli—infective pneumoconiosis. Infective pneumoconiosis has already been produced by the vole bacillus (*mycobacterium tuberculosis* var. *muris*) [*Ibid.*, 1959, v. 34, 239] and coal dust. BCG has been used with kaolin with similar results [*Ibid.*, 1955, v. 30, 241].

In animals injected with coal dust and vole bacilli there were lesions in both the untreated and those treated with Triton. In the untreated animals necrosis was present in the lesions as were also vole bacilli; with kaolin and vole bacilli, the lesions were on the whole less in the animals treated with Triton. Necrosis and vole bacilli were present in the untreated and not in the Triton-treated animals.

It has been found that weights of the trachea-bronchial lymph nodes reflect in a quantitative way the changes in the lungs. These were investigated and the results analysed statistically. The effect of the Triton on the animals injected with coal and vole bacillus was not significant, but in the animals injected with kaolin and vole bacillus,

the treated animals showed a mean weight of only half of that of the untreated animals. The inference is that the effect of Triton may depend on the infective pneumoconiosis produced by the particular dust.

Charles L. Sutherland

WORTH, G. Die "Staublung" des Kohlenbergarbeiters. [Pneumoconiosis in Coal-Miners] *Deut. med. Woch.* 1960, Feb. 5, v. 85, No. 6, 221-6, 6 figs. [Numerous refs.]

In this paper with its numerous references there is an account of the findings of investigations of pulmonary function of miners before and after a work shift, after experimental exposure to aluminium dust, and also of those miners who had been working for many years. There is also a considerable description of clinical observations in miners. The discussion emphasizes the difficulties of assessing the effects on health of exposure to a dusty atmosphere. These effects are of complex nature for contributory factors may be climate and atmospheric pressure, weather, cramped working conditions and increased susceptibility to colds. Impairment of pulmonary function in men working in dusty atmospheres cannot always be equated with silicosis.

M. E. Delafield

COTES, J. E. Respiratory Function and Portable Oxygen Therapy in Chronic Non-Specific Lung Disease in relation to Prognosis. *Thorax.* 1960, Sept., v. 15, No. 3, 244-51. [42 refs.]

Generally attempts to relate prognosis in chronic lung disease to the results of lung function measurements have been restricted to a limited number of tests [see for example, this *Bulletin*, 1959, v. 37, 136]. Such studies indicate which physiological tests have a prognostic value but provide limited information about their relative merits for this purpose. To help elucidate this, 2 groups of suitable cases were investigated.

Series A comprised 29 subjects who were followed up over a period of 3½ years. Of these 16 had progressive massive fibrosis of coalworkers' pneumoconiosis, 2 had simple coalworkers' pneumoconiosis, and 11 had no evidence of pneumoconiosis. All were considered clinically to have chronic bronchitis or emphysema or both, and, on electrocardiography, to have some degree of right ventricular strain. 69% of this group died during the course of the follow-up.

In Series B numbering 38 followed up for 1 year, 20 had progressive massive fibrosis, 9 simple pneumoconiosis and 9 had no evidence of pneumoconiosis; 16 showed evidence of right ventricular strain. Each patient was investigated after a period of in-hospital treatment at a time when he was free from any condition which might vitiate the tests.

The investigations included various measurements of pulmonary ventilation, perfusion and diffusing capacity before and after exercise (treadmill) and electrocardiographic examination and estimation of erythrocyte sedimentation rate and haemoglobin. Details of the actual methods are described. The results are set out in a series

of 9 tables, 3 indices of prognostic importance emerged. First, hypoxaemia and a greatly increased venous admixture; second, the ability to perform more exercise breathing oxygen than breathing air under standard conditions; and, third, ECG changes characteristic of pulmonary disease. Each factor may occur in isolation but more often there is a causal relationship between them.

The subjects with the poorest prognosis were those who initially had the greatest pulmonary ventilation perfusion inequality as judged ($P < 0.01$) by a high percentage venous admixture, a low arterial blood oxygen tension at rest which fell further on maximal exercise, and the ability to perform more exercise breathing oxygen than air. Electrocardiographic evidence of pulmonary heart involvement was also a bad prognostic sign.

Indices which had some prognostic value ($P < 0.10$) included the pulmonary diffusing capacity, the degree of hypercapnia on maximal exercise breathing oxygen, and the ventilation per unit of energy expenditure on exercise breathing air.

Indices of no prognostic value in this group of subjects included maximum breathing capacity, the total lung volume, its subdivisions, and the residual volume as a percentage of total lung capacity, the blood erythrocyte sedimentation rate of haemoglobin.

The data, it is suggested, lend limited support to the belief that a sheltered home life, reduced physical activity, and freedom from chest illness have a favourable influence on prognosis.

A. Meiklejohn

PERNIS, B. & VIGLIANI, E. C. Recenti acquisizioni sulla patogenesi della silicosi. [Advances in the Pathogenesis of Silicosis] *Med. d. Lavoro*. 1960, June-July, v. 51, Nos. 6/7, 427-41, 2 figs. [Numerous refs.] English summary.

The English summary appended to the paper is as follows:—

"Several theories on the pathogenesis of silicosis have been put forward in the past, namely: the mechanical theory, the solubility theory, and the theory of specific fibrogenic activity of the crystalline surface. None of them could explain the mechanism of production of the silicotic nodule with its hyaline core and its cellular halo. In the present paper the immunological approach to silicosis is summarized and an exploration is given of how it accounts for the humoral and morphological features occurring in experimental and human silicosis. The immunological theory as it has been worked out by the Institute of Occupational Health of Milan, with the collaboration of Institute of Pathology of Turin and the Institute of Anatomy of Milan is centred on the following facts:

"1) The hyaline substance of the silicotic nodule is composed of 30% collagen, 50% gamma-globulins, 17% lipids and 3% carbohydrates not containing exuronic acids. Therefore the non-collagen component of the hyaline substance is not in excess of the normal connective tissue ground substance but a pathological substance very similar to amyloid and to the fibrinoid which are found in some immunological diseases.

"2) In the developing silicotic nodule and in its

regional lymphnodes many cells of the plasmocytic series, i.e. antibody producing cells, are visible: the deposition of the hyaline substance runs parallel with the appearance of plasmocytic cells.

"3) In the blood of silicotic animals and often in that of silicotic workers a higher content of gamma-globulins exists and substances appear which are commonly seen during chronic immunological disorders (immunoglobulins, zymosan agglutinating factor, rheumatoid factor).

"4) When introduced into the organism quartz activates the reticulo endothelial system as shown by the carbon clearance method, and enhances the production of antibodies; its action is similar to that of endotoxin lipopolysaccharides.

"The first link of the chain of reactions leading to the development of the silicotic nodule seems to be the death of macrophages which have phagocytosed the quartz particles. There are reasons to believe that this death is due to the activation of the first component of the complement, or to the activation of the aspecific esterases contained in the macrophages. From the dying macrophages substances are set free which activate the reticulo-endothelial system, the antibody formation and the production of collagen fibres. Quartz therefore acts as a potent activator of all immunological responses and this activation accounts for the pathogenesis of the silicotic nodule. The Authors are convinced that quartz is neither an antigen per se nor is capable of denaturing the proteins so as to render them autoantigenic. Quartz pathology belongs therefore to the field of aspecific immunology and especially to the action of substances which kill macrophages and have a strong adjuvant activity, such as endotoxins or Freund's adjuvant."

CHVAPIL, M. & HOLECKOVÁ, E. The Effect of Different Concentrations of Silicic Acid and Silica Dust on the Biosynthesis of Collagen in Tissue Cultures. *Brit. J. Indust. Med.* 1959, Oct., v. 16, No. 4, 286-9, 2 figs. [18 refs.]

In these experiments the effect of substances stimulating fibrogenesis *in vivo* was investigated by measuring directly the synthesis of collagenous products *in vitro*. The methods in which embryonic chicken lung tissue was used are described. The ability of the cultures to produce collagen after 8 days of cultivation was first confirmed, hydroxyproline being used as the indicator of the amount of collagen. Cultures incubated with an inert dust (TiO_2) showed no effect. Silica dust inhibited collagen formation.

The effect of silicic acid varied with the concentration. In concentrations of 0.005M collagen formation was stimulated, at higher concentrations of 0.01M it was inhibited, at the very low concentrations of 0.001M it had no effect. The silica dust used in the experiment would dissolve in serum during 8 days to produce a concentration of the same order as the inhibiting concentration. The inhibitory effect of silica dust on collagen synthesis in tissue culture is due to its solubility in a serum medium.

The results found point to the conclusion that silicic acid in adequate concentration stimulates the activity of some enzymatic system of the cells which take part in collagen synthesis.

Charles L. Sutherland

CHARBONNIER, J., MOUSSARD, H. D., ISELIN, P. & SOULE, J. L. Action de la silice en solution sur le système enzymatique succino-deshydrogénase-cytochrome oxydase. [The Action of Silica in Solution on the Succinic-Dehydrogenase-Cytochrome-Oxidase Enzyme System] *C.R. Soc. Biol.* 1959, v. 153, No. 10, 1492-5. [10 refs.]

The work described in this paper was undertaken as a result of observations made by the authors in their researches by electron microscopy on the experimental formation of silicotic lesions, that in renal lesions abnormalities of the mitochondria were frequently seen and also that by histochemical techniques it was found that variations in the activity of succinic dehydrogenase occurred.

There is a description of the silica solutions prepared from quartz, amorphous silica, sodium silicate and silicic acid for testing with enzyme extracts derived from heart tissues of the horse. The results of experiments were negative as the different silica solutions in a concentration of 100 mgm. of SiO_2 per litre and a pH of 7.3-7.4 produced only an inconstant and slight (of the order of 5%) diminution in the respiratory activity of the succinic-dehydrogenase—cytochrome-oxidase system.

M. E. Delafield

ITO, M. & OSANAI, H. [Experimental Pneumoconiosis by the Dust evolved from the Electric Furnace of a Metallic Silicon Factory] *J. Sci. of Labour.* Tokyo. 1960, Aug., v. 36, No. 8, 415-17, 2 figs. [55 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"The dust evolved from the electric furnace of metallic silicon factory was infused intratracheally as suspension in Ringer's solution in rats.

"The dust contained 91% of total SiO_2 , which consists of about 15% of α -cristobalite, 4.5% of quartz and other amorphous type of silica. The dust showed in rats as strong fibrogenic activity as pure quartz dust.

"The dust evolved by burning silica can be found also as a component of material used in pottery or other manufacture, and the above mentioned fact suggests that attention should be paid to such a kind of dust, in order to prevent the occupational pulmonary disease."

NOJIMA, K. [Radiological Studies of Silicosis in a Copper Mine yielding High Silica Dust. Report 5. A Contribution to Differential Diagnosis of Silicosis and Associated Tuberculosis] *J. Sci. of Labour.* Tokyo. 1960, Aug., v. 36, No. 8, 432-8, 8 figs. [In Japanese.]

"A long-term observation was made to ascertain whether a prudent scrutiny could contribute to the differential diagnosis between simple silicosis and associated tuberculosis to some extent, and the results obtained were as follows:

"1. Tubercule bacilli were detected in the sputum of 71.4% (65 out of 91) of the cases with unilateral or asymmetrical changes of the early confluent stage, and in the

sputum of 21.6% (16 out of 74) of the cases with bilateral or symmetrical lesions of the same stage. They were far more frequently detected in the former.

"2. The frequency of positive discharge of tubercule bacilli was 83.3% (40 out of 48) in the cases showing unilateral or asymmetrical appearance of large confluent or massive shadows and 25.0% (7 out of 28) in those with bilateral or symmetrical lesions of similar aspects. It was far higher in the former.

"3. The discharge of tubercule bacilli was evidenced in 84.4% (76 out of 90) of the cases with unilateral confluent shadows and in 59.2% (29 out of 49) of those with bilateral but asymmetrical confluent shadows. The frequency of positive discharge was much higher in the former.

"4. These results suggest that the roentgenologic diagnosis of tuberculosis associated with silicosis is not utterly impossible, if the stage of progress of silicosis mentioned in the previous paper is taken into consideration and due attention is paid on the onset, form and site of massive shadows.

"5. The larger the amount of silica dust inhaled, the more difficult the differential diagnosis of associated tuberculosis, and the diagnosis is getting more complicated, owing to the chemotherapy.

"6. In cases of advanced silicosis with confluent shadows, accordingly, the chemotherapy should be tried regardless of whether tuberculosis is confirmed to be associated with it or not."

ANDERSON, J. & CAMPAGNA, F. A. **Asbestosis and Carcinoma of the Lung. Case Report and Review of the Literature.** *Arch. Environment. Health.* Chicago. 1960, July, v. 1, No. 1, 27-32, 5 figs. [20 refs.]

OCCELLA, E. & CHIESA, P. Étude sur l'empoussièrement dans une mine de sidérose. [Dusty Conditions in a Siderite Mine] *Med. d. Lavoro.* 1960, May, v. 51, No. 5, 359-68, 5 figs. English summary.

The paper describes a preliminary study of dust at working places in a siderite mine, where the rock is mainly micaceous and chlorite schists with an average of quartz schists.

Chemico-petrographic analyses were made of samples of the mined rock, of sedimented dust, and of airborne dust. Concentrations of the airborne dust were measured by means of a thermal precipitator, the samples being evaluated under a magnification of 200 diameters.

The mined rock contained about 20% of free crystalline silica. The fractions of both the airborne and deposited dusts below 5μ in diameter had a free-silica content smaller than that of the rock sample. In the headings the free-silica content of the fine dust was about 8%, whilst in the mining areas it was about 2 to 3%.

The maximal concentrations of airborne dust were about 2,000 particles per cc. in the headings, and 1,000 in mining areas. The maximal concentrations in the headings were only reached during drilling (with water flush). At such times only, the dust concentrations reached the maximum allowable level of 100 particles of quartz per cc. of air.

Thomas Bedford

GENOT, R. Enquête sur la byssinose. [Study on Byssinosis] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale*. 1960, May, v. 18, No. 5, 339-57.

In a cotton mill employing 474 people, 28 cardroom and 23 other workers were questioned about symptoms and had chest X-rays taken. The method of selection of these workers is not described. Symptoms of dyspnoea, dislike for smoking, cough and tightness of the chest and abnormal evening tiredness were found, mainly on Mondays. These symptoms were 4 times commoner in the cardroom workers than the others. There were no X-ray changes directly associated with these symptoms, though a few cases of emphysema were reported.

The author concludes that there are cases with the symptoms of byssinosis in the mill surveyed but cannot say whether these symptoms are associated with a disabling condition. No pulmonary function tests were done.

Suzette Gauvain

BELLINI, F. & FINULLI, M. Gastroduodenite ed ulcera peptica nel saturnismo. [Gastroduodenitis and Peptic Ulcer in Saturnism] *Med. d. Lavoro*. 1960, May, v. 51, No. 5, 369-75. [33 refs.] English summary.

This paper reports an investigation of a series of 457 patients who had been treated for lead poisoning at the Clinica del Lavoro, Milan, over a recent period of 15 years. There was a history of occupational exposure to the lead hazard in each case, with colic or other significant digestive disturbances and such positive laboratory findings as reduction of the red blood corpuscles, increase in the number of basophils, increased lead content in blood and urine, coproporphyrinuria. 268 patients had been examined by X-ray and 62 (13.5% of the whole series) showed evidence of a gastro-duodenitis; 18 (3.9%) had peptic ulcer. Classification by trade showed a fairly uniform distribution among some 10 different occupations where the lead hazard is known to exist. Changes in the gastric juice had been found in 129 out of 158 patients examined.

The authors believe that a repetition of local spasms, which occur in lead colic, may cause trophic changes in the gastro-duodenal mucosa and that this also suffers toxic damage because of lead being both absorbed by, and excreted through, it. They discuss the possible significance of lead poisoning in the pathogenesis of gastro-duodenal ulcer.

J. Cauchi

GRISLER, R. & FINULLI, M. Utilità della tecnica semplificata della clearance dell'acido paraamino-ippurico nello studio delle nefropatie vascolari professionali. [Use of Simplified Technique for p-aminohippuric Acid Clearance in Studying Occupational Vascular Kidney Diseases] *Med. d. Lavoro*. 1960, May, v. 51, No. 5, 376-80. [17 refs.] English summary.

Results of investigations in normal and hypertensive subjects, as well as in 20 patients with lead poisoning,

show that a reliable evaluation of renal blood flow was obtained by means of this relatively simple technique [BETTGE and SIMON, *Ztschr. f. ges. Exper. Med.*, 1955, v. 125, 116]. It is based on the decrease in plasma concentrations of p-aminohippuric acid (PAH) in relation to time after a slow injection—5 minutes—of 10 cc. of a 20% solution of PAH. Blood samples were collected at intervals of 7-8 minutes, in most cases starting 30 minutes after injection. The test was completed in little more than 1 hour without the disturbances of catheterization necessary in traditional methods of thiosulphate and PAH clearance.

In the 15 normal subjects the median renal plasma flow was 620 cc. per minute, range 530-780. With the traditional, more complex method, published figures are 640 cc. per minute, ranges 476-804 and 400-809, these wide ranges being attributed to variations in diuresis caused by the presence of the catheter.

Among 20 cases of hypertension of non-occupational aetiology, the renal plasma flow ranged from 170 to 840; in 13 it was less than 530, and 6 of these had a blood urea greater than 50 mgm. per 100 cc. Tables give, in addition, ages, blood pressures and urinary specific gravities for these patients and those with lead poisoning. Of 4 with lead colic, 3 had decreased renal plasma flow, and 1 hypertension. Of 5 who had had colic recently, 2 had decreased plasma flow and none hypertension. The plasma flow was normal in 3 with lead anaemia without colic; 1 had hypertension. Of 8 with chronic lead poisoning, 6 had decreased plasma flow, 4 of them with hypertension. The median plasma flow in these 4 groups with lead poisoning were 500, 560, 760 and 457 respectively.

The test, being easily and quickly performed, with little discomfort for the patient, is suggested for the investigation of occupational diseases with suspected vascular lesions since it provides a picture of renal function.

M. Patricia Fitzsimons

REUBER, M. D. & BRADLEY, J. E. Acute Versenate Nephrosis occurring as the Result of Treatment for Lead Intoxication. *J. Amer. Med. Ass.* 1960, Sept. 17, v. 174, No. 3, 263-9, 3 figs. [17 refs.]

It is recommended that the dose of calcium versenate should not exceed 75 mgm. per kgm. Treatment of Pb poisoning with 125 mgm. per kgm. for 3 days was followed 5 days later by uraemia, then by anuria. The patient, a 1-year-old girl, also had pneumonia and later pericarditis and bleeding from gums and gastro-intestinal tract. Kidney biopsy was performed 11 days after CaEDTA therapy ceased. Artificial haemodialysis 3 days later was followed by temporary improvement in clinical and blood biochemical findings. The patient died 3 days after this, and post-mortem findings were necrotizing broncho-pneumonia, with abscesses and thrombo-phlebitis in 1 lobe, acute nephrosis, pleuritis, pericarditis and cerebral oedema.

Biopsy had shown dilated proximal convoluted tubules with extremely flattened regenerating cells and some necrotic cells. The distal tubule cells were swollen, their nuclei were small; the lumen in places was collapsed or contained sloughed cells.

Autopsy showed the proximal tubular epithelium to be

less flattened; the lumen was dilated, lined by regenerating cells with occasional large nuclei. The distal tubular epithelium was vacuolated and swollen; in places the lumen was obliterated. The collecting tubules contained protein casts. Glomerular epithelial cells were large and contained coarse hyaline droplets with some destruction of tufts. Fat and inclusion bodies were not observed.

Liver, kidneys, spleen, lymph nodes and lungs contained no lead, blood and kidney no mercury. The blood originally contained 0.076 mgm. Pb per 100 ml.

Previously reported fatal nephrosis following CaEDTA is discussed [this *Bulletin*, 1957, v. 32, 870, 1171], and also the pharmacology, toxicity and dosage of this valuable drug. Tubular and glomerular lesions from heavy metals are described. The possible factor of the lung infection in mobilizing Pb is mentioned, and of chelation of trace metals on enzyme systems. Excretion and reabsorption of CaEDTA or some metabolite of the drug are believed responsible for the pathological findings. [See also this *ibid*, 1960, v. 35, 229].

M. Patricia Fitzsimons

ENNEKING, J. H. J. Hemolyse door vergiftiging met arseenwaterstof. [Haemolysis caused by Arsenic Poisoning] *Nederl. Tijdschr. v. Geneesk.* 1960, June 18, v. 104, No. 25, 1181-9, 5 figs. [24 refs.] English summary (8 lines).

The author describes 5 cases of arsine poisoning occurring in metal workers who inhaled arsenical fumes during smelting.

(1) A man aged 50 years, who became nauseated, vomited and passed dark red urine. Examination revealed increased bowel sounds and the urine contained blood and albumin. There was massive haemolysis, with a haemoglobin content of 43%, and liver function, as measured by the serum bilirubin, was impaired for 3 weeks. A 48-hour specimen of urine contained 280 μ gm. of arsenic. 1.2 gm. of BAL was given intramuscularly every 24 hours for the first few days. After 7 weeks the patient was discharged with a haemoglobin content of 71%.

(2) A man aged 40 years, who complained of colicky abdominal pain and dark urine. On examination he had a pyrexia of 39.2°C. and the urine was red and contained blood, albumin and amorphous masses of erythrocytes and leucocytes. Arsenic was detected in the urine. The serum was light red and contained methaemoglobin. The haemoglobin fell to 53%, and a blood transfusion was given; 1 month later it was 80%. He was discharged after 3 months.

(3) A man aged 39, who for 1 week had suffered from headache, tiredness and a sensation of coldness, followed by abdominal colic, nausea and vomiting. On examination there was jaundice and the bowel sounds were increased. The urine contained blood, bilirubin and urobilinogen in excess. The serum contained methaemoglobin. The haemoglobin content fell to 56% on the 8th day. He was treated with 200 mgm. of BAL intramuscularly 4 times a day for 2 days, and was discharged after 3 weeks.

(4) A man aged 35, with a previous history of hepatitis, who was anaemic and jaundiced. The urine con-

tained blood, albumin and bile, but there was no nausea or vomiting. After 9 days there was no excess of urobilinogen in the urine and by the 11th day the haemoglobin content was 83%.

(5) This patient complained of pain in the back and fleeting pain in the joints. The following day he had haematuria. He was not jaundiced and the urine did not contain bile; he became anaemic, with a red cell count of 2,830,000 per cmm. The course of the illness was uneventful and he recovered rapidly. *Anne Tohill*

MARCHAND, M. Parkinson manganique unilatéral. [Unilateral Parkinsonism Due to Manganese] *Arch. Malad. Professionnelles.* Paris. 1960, Sept., v. 21, No. 9, 571-2.

Report of a case.

CHOLAK, J. & HUBBARD, D. M. Determination of Manganese in Air and Biological Material. *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 356-60, 1 fig.

PAYNE, W. W. The Role of Roasted Chromite Ore in the Production of Cancer. *Arch. Environment. Health.* Chicago. 1960, July, v. 1, No. 1, 20-26, 1 fig. [18 refs.]

A specific risk of lung cancer among workers in chromate-producing plants has been established by studies in Europe, the U.S.A. and England. HEUPER [this *Bulletin*, 1959, v. 34, 138] and HEUPER and PAYNE [*Ibid*, 1960, v. 35, 26] have shown that squamous-cell carcinomas and sarcomas can be produced by the injection of roasted chromite ore intrapleurally and intramuscularly into rats and by the injection of pure chromium compounds.

In the present study, fractions of the residue from the first leaching of the chromite ore roast have been tested for carcinogenicity, and an attempt has been made to see if their effect is that of initiating or promoting cancer, by injecting the fractions alone and with benzopyrene. 4 sarcomas were produced among 70 rats by implantation of the whole residue intrapleurally or into the thigh. No sarcomas were produced by similar implantation into mice. 3 sarcomas were produced among 52 mice by subcutaneous injection of the whole residue containing particles less than 10 μ in size from which practically all water-soluble hexavalent chromium had been removed. No tumours were obtained by subcutaneous injection of the 5-10 μ fraction of the residue nor of the fractions less than 2 μ . Neither were any tumours produced by chromic phosphate.

Chemical analysis showed that the small particle residue contained the highest amount of water-soluble hexavalent chromium and this fraction alone produced a substantial number of early deaths from non-malignant conditions 0.05 mgm. of benzopyrene without any added residue produced tumours in 37% of mice. This proportion was reduced when the various fractions of the chromite ore residue were added and was most reduced with the

reactions containing the smaller particles and the higher proportion of hexavalent chromium.

It is concluded that intermediate products in the production of chromium chemicals and the discarded residue have a carcinogenic effect but no promoting effect. The inhibition of the effect of benzpyrene is thought to have been due to chemical reaction between the chromium compounds and the benzpyrene. It is noted that the doses of chromium compounds in the present experiments (less than 0.5 mgm. of hexavalent chromium) were substantially less than the dose used in previous experiments with pure chromium compounds (10 mgm.). The negative inhalation experiments reported by BAETJER *et al.*, *ibid.*, 1960, v. 35, 26] may be accounted for by the fact that the dose administered was limited by the acute toxic effects attributable to the hexavalent chromium content of the material used.

Richard Doll

SAMITZ, M. H., KATZ, S. & GROSS, S. **Nature of the Chromium extracted from Leather by Sweat.** *J. Occup. Med.* Chicago. 1960, Sept., v. 2, No. 9, 435-6.

Previous experiments having shown that chrome-tanned leathers and sweat extracts of these leathers contained both trivalent and hexavalent chromium, the chromium in the extracts was investigated by spectrophotometric analysis, after suspended material was removed by centrifuge. This material also contained chromium and is being studied.

Reference curves were prepared for 8 standard solutions of chromic salts, basic chrome sulphate, chromates or dichromates, containing 100 μ gm. chromium per ml., the approximate concentration of the sweat extracts. From absorption spectra data obtained from the standards in the 350-950 millimicron range, it was possible to assign characteristic maxima and minima to the various forms of chromium. Another table gives data for 10 extracts, and also for sweat. All the extracts showed maxima at 350 and 425-430—due to the chromate ion, and at 475-520 and 765-950—due to the sweat, and a minimum at 695-705, due either to the hydrated chromic ion, the basic chrome sulphate complex, the chromate ion or the sweat. Some extracts showed, in addition, a maximum at 580, due to the complex.

It is concluded that the trivalent chromium extracted from the leathers was in the form of a basic chrome sulphate complex similar to the sample studies [this *Bulletin*, 1959, v. 34, 355] and that the hexavalent chromium was in the form of the chromate ion [See also *ibid.*, 1960, v. 35, 113.]

M. Patricia Fitzsimons

LINDEKEN, C. L. & MEADORS, O. L. **The Control of Beryllium Hazards.** *Amer. Indust. Hyg. Ass. J.* 1960, June, v. 21, No. 3, 245-51, 4 figs. [14 refs.]

This short paper describes how some operations involving powdered beryllium oxide and the machining of elemental beryllium have been partially or completely enclosed to reduce air contamination. The method of routine air sampling is described.

C. H. Wood

KOKOREV, N. P., BOBRISHEV-PUSHKIN, D. M. & KRANTSFELD, V. D. [Problems of Occupational Hygiene in the Production of Titanium] *Gigiena Truda i Professional'nye Zabolevaniya*. Moscow. 1960, v. 4, No. 10, 23-9, 1 fig. [12 refs.] [In Russian.]

The English summary appended to the paper is as follows:—

"Hygienically the production of titanium is characterized chiefly by dust formation in the raw materials preparation departments, evolution of chlore and especially of tetrachlorated titanium in the chloration and rectification departments and by a discharge of magnesia and magnesium chloride in the reduction and separation divisions of the plant.

"The tetrachlorated titanium is subject to hydrolysis in the air medium with a successive formation of a series of products, which tend to irritate the mucosa of eyes and upper respiratory tract, and being active for a lengthy time may produce toxic bronchitis. The largest masses of tetrachlorated titanium appear during dismantling of equipment and pipe-lines for repairs and cleaning. Basic sanitary measures to be carried out in the departments for the preparation of raw materials provide for prevention of dust discharge by creating effective sealing of the equipment, wetting and aspiration. In chloration and rectification departments these measures should include reduction of repairs. When planning the floor lay-out for these departments and disposition of the machinery therein consideration is to be given to the maximal sanitation and high-standard working conditions, rational ventilation, securing proper disposal of gases at the time of dismantling, organization of recreation and rest rooms, etc. In the reduction and separation departments recommendation is made to provide maximum isolation of the processes involving evolution of large gas volumes, along with the mechanization of the most harmful processes."

LANDRY, A. S. **The Polarographic Determination of Thallium in an Atmospheric Sample.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 407-13, 6 figs. [10 refs.]

SCHUMACHER, H. & GRANDJEAN, E. Vergleichende Untersuchungen über die narkotische Wirksamkeit und die akute Toxizität von neun Lösungsmitteln. [Comparative Investigations of the Narcotic Potency and Acute Toxicity of Nine Solvents] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 2, 109-19, 1 fig.

The narcotic effect on animals of a group of solvents widely used in industry was chosen as the criterion of their affinity for the central nervous system, and correlated with their acute toxicity as estimated by the LD50 by intraperitoneal injection.

The solvents investigated were benzol, toluol, xylol, methylene chloride, chloroform, trichloroethylene, tetrachloroethylene and propionic acid ethyl ester; a toluol-xylol 2+1 mixture was also included.

The narcotic potency was estimated by the time of onset of paralytic symptoms in 9 female rats exposed to an initial concentration of 15,000 p.p.m. (Stage I narcosis); the time of complete loss of reflexes (Stage IV narcosis), and the time of recovery under stimulation every 10 seconds by an electric current. Each animal was tested with a different solvent every 2 days for a week. For estimation of LD50 500 mice were used.

All the solvents caused some initial respiratory dyspnoea. With the chlorinated hydrocarbons there was a characteristic posture ("cat curve") but less frequent mucous membrane irritation than with the aromatic hydrocarbons; with methylene chloride there was obstinate biting of the bars of the cage; benzol was characterized by a special central nervous system effect—tremors, convulsions and spasms.

The average LD50 was lowest with methylene chloride (0.35 ml./kgm.) and highest with tetrachloroethylene (3.3ml./kgm.), but this criterion of acute toxicity showed no correlation with the narcotic potency, since the strongest affinity for the central nervous system was found with chloroform, trichloroethylene, tetrachlorethylene, and benzol, and the lowest with xylol and the propionic acid ester, the toluol-xylol mixture and methylene chloride being intermediate. The acute toxicity of the chlorinated hydrocarbons decreased as their chlorine content increased, that of the aromatics with an increase in the methyl group.

The only essential difference in time of onset of narcosis was shown by xylol and the ester, that of xylol especially being much longer delayed in both stages, indicating a wider range between light and severe narcosis than in the other solvents.

Those solvents with a short exposure time of onset had also a short recovery time; a lower affinity for the central nervous system was correlated with a longer recovery time.

Statistical examination of the effect on onset of narcosis of time of exposure and volatilization showed no significance in Stage I; time of exposure was significant only between xylol and the propionic ester in Stage IV.

Solvents with high central nervous system affinity are considered specially unfavourable from the point of view of accidents and acute poisoning. No assessment of chronic toxicity could be made from these results.

Ethel Browning

KUBOTA, J., ISHIZU, S. & MITSUHASHI, T. **Outbreaks of Benzene Poisoning among Home Industry Workers.** *Rep. Inst. Sci. of Labour.* Tokyo. 1960, July, No. 56, 11–17, 6 figs.

This survey, undertaken by the Institute, was part of a larger one of 817 vinyl sandal makers in Tokyo in 1959, when 42% had abnormal blood counts. Benzene poisoning from the glue had presented a social problem before in 1958, and also in Osaka in 1957, when 83% of 213 workers had anaemia or leucopenia.

Some details are given of 41 men and 59 women, employed in small mills or in poor homes, producing vinyl paste, making shoes or toys or gluing soles to shoes and sandals. Benzene concentrations above paste containers were 80 p.p.m., above glue containers more than

400 and at face level 5 and 120. Photographs show open containers on work tables and a pile of sandals drying in a room corner.

Preliminary screening depended on 4 sets of criteria, 2 each for men and women, according to the specific gravity of blood and red and white cell counts, and 11 men and 23 women had abnormal findings. Those below the lower criteria were referred for full haematological and marrow investigation. No details are given of the results of urinary investigations or enquiries concerning symptoms which were included in the survey plan. The home workers were more affected than regularly employed industrial workers, and many had anaemia rather than other abnormalities. Full details of blood and marrow examinations in 4 of them show, in addition to anaemia, thrombopenia and leucopenia or splenomegaly and thrombopenia or panmyelopathy, indicating that benzene, rather than poor nutrition, was responsible. The 34% affected were less than in other teams' surveys, possibly because this survey started later, when some sandal workers had already been suspended from work and others had started to use benzene substitutes.

M. Patricia Fitzsimons

KUBOTA, J. **Studies on Chloronitrobenzene Poisoning.** *Rep. Inst. Sci. of Labour.* Tokyo. 1960, July, No. 56, 1–10, 18 figs.

Examinations of Heinz bodies, formed during chloronitrobenzene (CNB) poisoning in rabbits, are illustrated and briefly discussed. The other toxic effects were methaemoglobin formation and anaemia and after investigating these 3 effects, Heinz body formation was considered as portraying the course of events which lead to haematuria, haemoglobinuria and anaemia.

After injection of CNB, methaemoglobin levels rose and fell in the first 12 hours and did so again in the second, but Heinz bodies remained at the peak which they had taken 18 hours to reach. In oxalated blood, collected early, methaemoglobin disappeared or decreased after standing, but it persisted or decreased only slightly after collection during the second increase. Heinz body formation was considered to have some relation to this persistence.

Various stained preparations of Heinz bodies are reproduced. After injection or skin application of CNB, they increased also in size and measured 1–2 μ in each erythrocyte observed in 18–24 hours. Under the electron microscope they were anelastic with high density of the order of that of the surrounding haemoglobin.

Haemolysed blood—collected when the Heinz bodies were beginning to form—after centrifuging and standing for 24 hours contained increased Heinz bodies in the sediment, within and without erythrocyte membranes. This did not happen when the supernatant had been removed immediately and the sediment washed and kept under saline. These findings and another filtration experiment, suggested that some haemoglobin was necessary for the completion of Heinz bodies. A day or so after poisoning, spectral analyses showed haemoglobin changes in the Heinz bodies, but not in the supernatant from which they were removed.

Their fate and excretion are implied in the destruction

of erythrocytes containing them, and histological pictures show what happened in spleen, marrow and kidneys. Degeneration of haemoglobin and haemoglobinuric nephrosis demand that poisoning should be prevented. Treating the methaemoglobinemia is not enough. [This paper gives few experimental details except as condensed descriptions of the figures.] *M. Patricia Fitzsimons*

EICH, J. Arbeitssicherheit beim Umgang mit Zweikomponenten-Kunststoffen. [Safety Measures for Workers with Two-Component Plastics] *Zent. f. Arbeitsmed. u. Arbeitsschutz*. 1960, Sept., v. 10, No. 9, 205-12, 1 fig. [16 refs.]

The rapid and extensive developments in the plastics industry have led to the position that the possible dangers to health of those who work with or in the production of these materials receive only secondary consideration.

This paper is concerned with 3 groups of plastics—polyurethane, epoxy resins and unsaturated polyester resins which are called two-component plastics because they are produced when and where required by the rapid interaction when mixed of 2 components each of which can be stored separately for months. An example of this is the 2-component adhesives of very great strength which are used for many purposes.

There is much chemical detail of the great number of substances used in the production of these plastics with reference also to the toxic irritant effects they may have on the respiratory and other systems, on the eyes and on the skin.

At the end of the paper there is a long and valuable summarized statement of many technical, medical, sanitary and personal measures which should be organized for the protection of the workers. *M. E. Delafield*

BOIKINA, B. S. & PEREGUD, E. A. [On the Presence of Free Epichlorhydrin in Epoxid Resins and Quantitative Methods of its Determination.] *Gigiena Truda i Professional'nye Zabolevaniya*. Moscow. 1960, v. 4, No. 9, 40-44. [In Russian.]

Epoxy resins are polymers, made generally by heating epichlorhydrin and diphenylolpropane in an alkaline medium. Depending on the conditions of the reaction the products might have a molecular weight of 350 to 4,000. Mention is made of 3 sorts of epoxy resins ED5, ED6 and E37 having different molecular weights.

Industrial processes involving heating of the epoxy resins are accompanied by the release of "deleterious substances" whose composition has not yet been worked out. The authors determined the quantity of epichlorhydrin obtainable from epoxy resins. The two methods used are described in detail. Essentially, in the first, epichlorhydrin is oxidized by iodic acid to formaldehyde which is estimated colorimetrically, in the second method epichlorhydrin is extracted by distillation with benzene, and after burning, the amount of halide is determined. Comparable results were obtained when batches were tested by the two methods.

With resin ED5 (of low molecular weight) from 0.32% to 0.77% of epichlorhydrin was found in different batches

and 0.07% and 0.13% on "experimental models". Resin ED6 yielded 0.21% and 0.27% from different batches.

It is concluded that as raised temperatures are involved in processes with epoxy resins practical measures for the removal of toxic mixtures in the atmosphere of industrial premises should be carried out. *W. R. Lee*

LARSEN, K. A. Forgiftning med insecticider (irreversible cholinesterasehemmere). Forgiftningsmåte og profylakse. [Poisoning from Insecticides (Irreversible Cholinesterase Inhibitors)] *Nordisk Med.* 1960, Nov. 10, v. 64, No. 45, 1415-20. [18 refs.]

The English summary appended to the paper is as follows:—

"Three fatal cases of poisoning from irreversible cholinesterase inhibitors are reported. Two of the cases were suicides and one was an accident. Data of 18 cases of poisoning from irreversible cholinesterase inhibitors reported in the Scandinavian literature are presented in tabular form.

"The modes of poisoning and the prophylactic problems are discussed. There are three ways to prevent these poisonings:

"1) Restrictive control of the sale and the use of these insecticides, including courses to inform the workers about the toxicity of the substances and how to use them;

"2) Introduction of less toxic insecticides;

"3) Prompt, effective and specific treatment of the poisoning, especially with the use of atropine and cholinesterase reactivators like Pyridin-2-aldoxime-methiodide (PAM)."

KANTEMIR, I., GENER, S., KAYAALP, O. & TIMLIOGLU, Ö. Experimental Studies on Hexachlorbenzene and Organic Mercurial Compounds which are used to protect Wheat Seed from Fungal Diseases. *Türk İjiyen ve Tecrübi Biyoloji Dergisi*. Ankara. 1960, v. 20, No. 1, 31-6. [Fuller version in Turkish 19-30, 2 figs.]

— & TIMLIOGLU, Ö. Experiments on Acute Toxicity of Hexachlorbenzene Preparations used to protect Wheat Seed from Fungal Disease. *Ibid.*, 45-9. [Fuller version in Turkish 37-44.]

—, CAM, C. & KAYAALP, O. Investigations and Observations on Two Diseases: Kara Yara and Pembe Yara which are observed in the South-East Part of Turkey. *Ibid.*, 79-83. [Fuller version in Turkish 51-77, 22 figs. on 5 pls. (13 refs.)]

[An abstract of these papers appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 130.]

TOUGH, Ishbel M., BUCKTON, Karin E., BAIKIE, A. G. & COURT-BROWN, W. M. X-Ray-Induced Chromosome Damage in Man. *Lancet*. 1960, Oct. 15, 849-51, 3 figs.

It was first observed by FLIEDNER *et al.*, (*Acta Haematol.*, 1959, v. 22, 65) that chromosome changes can be produced in man by means of ionizing radiation; this was

after accidental exposure to a mixed neutron gamma ray beam. The changes observed were a "stickiness", clumping of the chromosomes and anaphase bridge-formation in samples of the marrow in squash preparations. The present authors have had the opportunity of studying any such changes in two patients who were given X-ray treatment for ankylosing spondylitis. The chromosome preparations were made from blood cultures, by an adaptation of the technique of HUNGERFORD *et al.* (*Amer. J. Human Genetics*, 1959, v. 11, 215), the final spreading of the chromosomes was achieved by drying in air. With this technique a count of the chromosomes in 205 cells from 6 normal subjects showed 190 cells to have 46 chromosomes each (92.7%).

The first patient received treatment to the whole length of his spine and to his sacro-iliac joints. A total skin dose of 1500 rads was given in 10 equal fractions. The technical details were KV.250 on A.15, half-value layer 2.7 mm. cu. focus-skin distance 50 cm. Considerable chromosome damage was observed and there was a significant change in the count distribution.

The second patient was given only one dose of X-rays (250 rads) but 24 hours later there were two significant changes. The percentage of cells with 46 chromosomes had fallen from 93 to 72 and that of cells with structurally abnormal chromosomes had risen from 1 to 22.

In both patients unusual numbers of polyploid cells were seen. The altered chromosomes are well illustrated in two microphotographs.

S. Russ

ärztl. Fortbildung. 1960, Sept. 1, v. 54, Nos. 17/18, 1040-46. [23 refs.]

In this paper the author discusses the subject of eczema occurring in occupations in relation to the legal enactments in East Germany concerning the reporting and compensation of the disease. It may be difficult to form an opinion on whether the skin condition which may be of several different types is caused by the occupation or not. In the literature a number of different names have been assigned to occupational eczemas but these are here particularly considered in 3 groups—hyper-sensitivity, degenerative and sensitivity eczemas. Difficulties in the interpretation of the regulations are also discussed.

There are statistical tables which set out the experience in Leipzig in the period 1950-55 of medical notifications of occupational eczema, and of suspected occupational eczema. The total number of all these cases was 893 of which 571 were in males and 322 in females. There is an analysis of these by age and occupation. 305 persons suffering from various types of eczema were examined at the skin clinic by tests of the sensitivity and function of the skin.

There is a short account of the measures which should be taken in the endeavour to prevent occupational eczema.

M. E. Delafield

MORRIS, G. E. **The Primary Irritant Nature of Cement.** *Arch. Environment. Health.* Chicago, 1960, Oct., v. 1, No. 4, 301.

"A report is made of two cases of foot ulcer resulting from cement being in contact with the skin in localized areas for long periods of time."

SCHIMPF, A. Erfahrungen bei der Begutachtung beruflich bedingter Ekzeme. [Experience of the Assessment of Occupational Eczema] *Ztschr. f.*

Food and Nutrition

The order in this section is:—General; Foodstuffs; Food Poisoning.

FOODSTUFFS

(Composition and Bacteriological Control)

ANDERSON, E. S. **The Occurrence of *Salmonella paratyphi B* in Desiccated Coconut from Ceylon.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Sept., v. 19, 172-5.

37 cultures of *Salmonella paratyphi B* isolated from Ceylonese desiccated coconut were received at the Central Enteric Reference Laboratory, Colindale, London, between December 1959 and May 1960. The following phage types were represented: Beccles (8), 1 var. 9 (6), Dundee (3), Dundee var. 1 (2), Beccles var. 1 (1), Jersey (1), and Taunton (1). 15 were untypable. All the iden-

tified types have been found in human infections in Britain but with an order of frequency different from that found in the coconut. An outbreak due to a new phage type, 1 var. 9, in a hospital, was probably due to desiccated coconut, and the new type was isolated from this material. The source of the *Salm. paratyphi B* in coconut is considered to be human, the contamination occurring during manufacture in the country of origin. The author directs attention to Chinese frozen egg and coconut as sources of *Salm. paratyphi B*, and urges more effective control of imported foodstuffs.

[See also this *Bulletin*, 1960, v. 35, 1184.]

Betty C. Hobbs

HOBBS, Betty C., REEVES, Janet C., GARSIDE, J. S., GORDON, R. F., BARNES, Ella M., SHRIMPTON, D. H. & ANDERSON, E. S. **Antibiotic Treatment of Poultry in relation to *Salmonella typhi-murium*.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Oct., v. 19, 178-93. [23 refs.]

Known phage types of *Salmonella typhi-murium*, sensitive and resistant to chlortetracycline were fed to day-old chicks which were killed 10-12 weeks later and deliberately processed according to the worst examples of commercial practice. Test groups of the dressed poultry were totally immersed in slush ice containing 10 p.p.m. chlortetracycline (acronization), and together with control groups dipped in slush ice without chlortetracycline, were frozen; skin samples were examined for total and salmonella counts after storage of the hawed carcasses for 1, 2, 3, and sometimes 5 days at 5°C., and in one experiment, 22°C. also.

Acronization inhibited the growth of strains of *Salm. typhi-murium* sensitive to chlortetracycline and also of spoilage organisms for approximately 24 hours compared with controls. A strain of *Salm. typhi-murium* resistant to chlortetracycline grew readily on the skin of acronized and control poultry at 15°C. At 22°C. the growth of the resistant strain on acronized poultry was enhanced, compared with that of the non-treated controls.

It was concluded that salmonellae resistant to chlortetracycline were likely to grow at the expense of spoilage organisms on the skin of acronized poultry and render dangerous carcasses which would otherwise have been rejected, particularly as 81% of households in the United Kingdom are without refrigeration so that food is stored at atmospheric temperatures. *Salm. typhi-murium* was isolated from a high proportion of offal, cavity swabs, and skin of infected poultry and also from trays and slush ice.

There was a gradual development of resistance to chlortetracycline in sensitive strains of *Salm. typhi-murium* fed to chickens in diets containing 25-100 gm. of the antibiotic per ton. The mortality rate in antibiotic-chicks was approximately half that of control groups, but more carriers persisted in the test groups.

Of 627 strains of *Salm. typhi-murium* isolated in 1957-1959 in the United Kingdom from man, animals and food, 10 (1.6%), were resistant to chlortetracycline; a higher proportion of resistant strains is reported from the U.S.A. where there is more widespread use of chlortetracycline for animal feeding.

Betty C. Hobbs

BREIJER, H. B. G.; JULIUS, H. W.; BOS, F. J.; VAN THIEL, P. H.; KLOOSTERMAN, W.; BURG, A. **Experiments in the Disinfection of Raw Lettuce. Part. I. Bacteriological Aspects** [BREIJER, JULIUS & BOS]. *Trop. & Geograph. Med.* Amsterdam. 1960, June, v. 12, No. 2, 149-61. [17 refs.] **Part II. Parasitological Aspects** [VAN THIEL, BREIJER, KLOOSTERMAN & BURG]. *Ibid.*, 162-72.

I. These papers are from the Medical Department of Royal Rotterdam Lloyd and the Laboratory of Hygiene, University of Utrecht, and it seems that the object of the work described was to find a suitable method for disinfecting lettuces of possibly contaminated origin aboard ship. Some of the literature of the subject is first reviewed. The authors' own experiments were begun with lettuces grown in the Rotterdam Zoo and "watered daily with liquid manure obtained from buffaloes and bison under the supervision of the conservator of the gardens". This proved unsatisfactory because *Escherichia coli* was removed from them by simple washing. They therefore sprayed dilute culture on lettuce leaves and allowed it to dry: when these were put through a blank test (which included homogenizing the leaves in a blender after treatment) 25% or more of the organisms were recovered.

Their own first tests were done with a solution of which they got news from a press report: this stated that American soldiers in Berlin were forbidden by the U.S. Army Command to eat lettuce unless it had been treated with DCFS (Disinfectant, Chlorine, Food Service). This contains trichloromelamine, sodium dodecyl benzene sulphonate (NDBS) citric acid and phosphoric acid. Some was obtained and a 1.25% solution was found to eliminate *E. coli* from lettuce at room temperature in 30 minutes or less. However, DCFS is expensive, and attempts were made to find a cheaper disinfectant with the same effect. After various experiments it was decided that an equally effective solution was 0.3% NDBS and 2% Halamid (sodium *p*-toluenesulphon-chloroamide, i.e., chloramine-T). Immersion in this for half an hour at 15°C. regularly killed *E. coli*; *Salmonella typhi* was shown in simple tube tests to be killed more rapidly than *E. coli* by Halamid.

II. This study was made with cultivated (DOBELL's medium) *Entamoeba invadens* (a reptilian species) and *Entamoeba histolytica*. Cyst suspensions were exposed to disinfectants either in tubes or dried on lettuce leaves, and survival or death was determined by cultivation. The conclusion is reached that the solution of Halamid and NDBS (above) is actually superior to DCFS in destroying cysts, and that treatment of lettuce with this solution at 25°C. for 30 minutes should suffice. [The results obtained by this difficult technique are somewhat erratic, but a few positive cultures were in fact obtained after this treatment, and the argument that these cultivated cysts may have been more resistant than would be those deposited from an excremental source, because they were covered with starchy slime from the medium, is perhaps a little optimistic.]

L. P. Garrod

DAVIS, J. G. **Milk Testing. The Laboratory Control of Milk.** 2nd Edition.

This book was reviewed on p. 103.

FOOD POISONING

BEECHEY, H. T. **Some Practical Aspects of Food Poisoning in Nairobi.** *Sanitarian*, London, 1960, Oct., v. 69, No. 1, 6-14.

The author, who is Chief Health Inspector, Nairobi City Council, points out that the true incidence of food poisoning in Nairobi is unknown because the disease is not notifiable.

15 outbreaks involving approximately 672 persons have been reported and investigated during the last 6 years, and these are described. 7 were confirmed as dysentery (*Sh. sonnei* (6) *Sh. manchester* [*Sh. flexneri* 6] (1)) and 4 others were thought to be dysentery but were not con-

firmed bacteriologically; carriers were usually found. 2 outbreaks were thought to be due to staphylococcal enterotoxin: a throat carrier was blamed in one instance, and milk in the other, but the strains of staphylococci were not phage-typed.

Comparing these figures with incidents of food poisoning in England and Wales the author is surprised that no outbreaks of salmonella or *Cl. welchii* food poisoning had been recorded in Nairobi. [The history of incidents 10 and 15 resembles that common to *Cl. welchii* food poisoning in England.]

An outbreak due to poisonous fungi is described.

Personal and kitchen hygiene is discussed in relation to the incidents.

Betty C. Hobbs

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma; Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

FARRIS, G. & LERZA, P. *Sulle micosi cutanee tra i lavoratori di una azienda di trasporti urbani. [Cutaneous Mycosis among the Workers of an Urban Transport Firm]* *Rass. Med. Indust.* Turin, 1960, Mar.-Apr., v. 29, No. 2, 89-98, 2 figs. [23 refs.] English summary.

The authors have had the medical care of the staff of a transport undertaking for the period of 7 years. They recorded 1,183 cases of skin complaints (not including such conditions as abscess, fistula, venereal rashes, etc.) and found 165 (13.9%) of these to be mycoses, which affected the feet in 105 (63.6%). They also dealt with skin complaints in 625 family contacts of the staff: 27 (4.3%) were mycoses, 4 (14.8%) affecting the feet.

The total strength of the staff employed is not stated. The skin mycoses affected 9 working in the offices, 67 travelling staff (drivers, conductors, etc.) and 89 mechanics, cleaners and others who work in the garages and depots and who make much use of the showers there provided.

Candida albicans and *Trycophyton rubrum* have been isolated from the patients and *Cephalosporium acremonium* and *T. rubrum* from scrapings taken off the floors and duckboards of the shower baths. *J. Cauchi*

NEWCOMER, V. D., HOMER, R. S., REISNER, R. M., SORENSSEN, L. J., McNALL, E. G. & STERNBERG, T. H. **The Treatment of Tinea Capitis with Orally Administered Griseofulvin.** *J. Dis. Children.* Chicago, 1960, May, v. 99, No. 5, 585-96, 5 figs. [38 refs.]

After reviewing previous reports on therapeutic trials with orally administered griseofulvin, the authors record the results which they themselves achieved with this drug when they administered it orally to 49 patients presenting with tinea capitis and other lesions.

The drug was administered 4 times daily, the dosage being calculated on a weight basis (patients weighing more than 27.5 kgm. were given 1gm. daily and patients weighing less than 27.5 kgm. were given 20 mgm. per kgm.). Before treatment, fungi isolated in culture from the lesions were typed. The causative fungi isolated from these lesions were distributed among the cases as follows: *Microsporum audouini* 23 cases; *M. canis* 15; *Trichophyton tonsurans* 10; and *Epidermophyton floccosum* 1 case.

The patients were interviewed at weekly intervals, and were questioned concerning possible side-effects of the treatment administered to them. Serial blood counts were also carried out on these patients.

The response to treatment was favourable in all cases due to *M. audouini* (subsidence of erythema, scaling, induration, disappearance of fluorescence of the infected hairs, and definite evidence of return of normal hair growth) and this occurred within 3 to 9 weeks. In the majority of cases clinical cure was achieved in 4-7 weeks. During this period the fluorescence of the hair faded to "a flat chalky hue" as well as being relegated to the distal part of the growing hair shaft. *M. canis* infections responded similarly.

Difficulty was experienced in assessing the effects of treatment in cases of tinea capitis due to *T. tonsurans* which does not cause fluorescence in the affected hair shaft. In these cases assessment of clinical cure (obtained

in 3-9 weeks) was based on "loss of scaling and disappearance of 'black dots'".

No significant toxic effects were experienced by any of the patients in this series. *C. J. La Touche*

THORNE, N. & HARVEY, K. M. **A Clinical Evaluation of the Fungicidal Properties of 5-Chloro-2 (*p*-Diethylaminoethoxyphenyl) Benzthiazole.** *Post-graduate Med. J.* 1959, Dec., v. 35, No. 410, 696-8.

In view of previous [as yet unpublished] claims that 5-chloro-2 (*p*-diethylamino-ethoxyphenyl) benzthiazole was active *in vitro* against fungi and bacteria, the authors of this report decided to conduct a clinical trial of this substance.

22 patients suffering from various superficial fungal infections provided the material for this trial. The sites affected were: "scalp 8, face 2, hands 2, trunk 3, arms 2, buttock 2, groins 2, legs 3, feet 12 and nails 6". In some patients several of these sites were affected. The infection had been present for 3 weeks to 10 years in the 19 in whom the duration was known.

13 of the patients had received some treatment with other drugs previously.

The results obtained showed that while this substance did not possess a greater therapeutic value than any of the topical drugs in current use, its side effects were negligible. The findings are tabulated in detail. *C. J. La Touche*

ZÓŁKIEWICZ-RODZIEWICZ, Helena. Leczenie grzybicy strzyżącej kwasem salicylohydroksamowym. [The Treatment of Ringworm with Salicylohydroxamic Acid] *Ann. Univ. Mariae Curie-Skłodowska.* Lublin. Sect. D. 1959, v. 14, 267-70.

The English summary appended to the paper is as follows:—

"At the Dermatological Clinic, Medical Academy, Lublin, 73 patients affected with ringworm were treated with salicylohydroxamic acid. 51 of the patients were affected with profound ringworm of the scalp, 15 with profound ringworm of the beard, 2 with superficial ringworm of the scalp and 5 with ringworm of the body. In 12 patients affected with profound ringworm of the scalp, superficial ringworm of the body was also found. Among the patients, aged from 2 to 67, there were 55 children, 16 men and 2 women.

"The dose of salicylohydroxamic acid for adults was 1 to 2 g per day, and for children 0.03 g per kg of body weight. The total dose administered ranged from 10 to 70 g. It averaged from 15.0 to 25.0 g for children and 35.0 to 45.0 for adults. The patients were treated for 20-30 days. The shortest period of treatment was 14 days, the longest 46 days. No toxic or allergic symptoms were observed during treatment.

"The drug proved effective in 71 patients affected with profound ringworm of the scalp, beard and body. In 2 patients affected with superficial ringworm of the scalp the drug was ineffective. Further investigations are now being carried out."

LITTLE, J. A. & STEIGMAN, A. J. **Erythema Nodosum in Primary Histoplasmosis.** *J. Amer. Med. Ass.* 1960, June 25, v. 173, No. 8, 875-7, 3 figs.

In this report further prominence is given to the association of erythema nodosum with histoplasmosis [see also this *Bulletin*, 1959 v. 34, 1116].

This allergic phenomenon was observed in a girl aged 6½ years who had been admitted to hospital because of a pulmonary lesion seen on X-ray examination. Tests for tuberculosis were negative, but a skin test with a 1:100 dilution of histoplasmin was positive. Erythematous swellings appeared on her forehead. They disappeared in 2 days, but reappeared on the forehead and also on the wrist after a 4-day interval.

"Painful pretibial nodules" were also observed in a girl aged 2 years. In this case also skin tests with histoplasmin were strongly positive, but they were negative with PPD.

In a boy aged 7½ years presenting with "fever, sore throat, and generalized aching" a "typical eruption of erythema nodosum" was observed. Again, skin tests were strongly positive with histoplasmin and negative with PPD.

Lastly, erythema nodosum was observed in a boy aged 2¼ years who, 1 week previously, had developed "an intermittent, low-grade fever and had become anorectic." As in the other 3 cases, this patient responded positively to a skin test with histoplasmin, but negatively with PPD.

C. J. La Touche

SALIBA, A. & BEATTY, O. A. **Pulmonary Histoplasmosis. Importance of Diagnostic Methods, with Report of an Early Case.** *J. Amer. Med. Ass.* 1960, June 25, v. 173, No. 8, 902-4, 5 figs.

In order to emphasize the importance of including the possibility of histoplasmosis in the differential diagnosis of suspected but not confirmed cases of tuberculosis the authors of this article report the full case history of one of their patients as an example, and also the chief relevant data of 8 others. In all these the pathologist's report supported a diagnosis of tuberculosis, but a mycological study of histological sections stained by special techniques revealed the presence of *Histoplasma capsulatum*. From some of these patients also this organism was recovered in culture from the sputum. *C. J. La Touche*

FORSEE, J. H. & PFOTENHAUER, M. **Surgical Management of Focalized Pulmonary Histoplasmosis.** *J. Amer. Med. Ass.* 1960, June 25, v. 173, No. 8, 878-83, 6 figs. [14 refs.]

In order to forestall the spread of a possibly malignant pulmonary lesion, thoracotomy was performed on 57 patients in whom X-ray investigations had revealed a focalized pulmonary lesion. These patients, whose ages ranged from 18 years to 40 years were on the whole asymptomatic, but tests with histoplasmin were positive in 51 of 52 who were thus tested. Histological material removed at operation revealed *Histoplasma capsulatum* in every case.

During the immediate post-operative period progress

was satisfactory in the majority of cases; but in 2 cases complications of major significance developed which required further surgical intervention, while in 4 others thoracentesis had to be performed "on more than one occasion", and in one case an abscess which developed post-operatively required drainage for a period lasting 4 months.

A reassessment of the health of these 57 patients 2 to 7 years after operation revealed that "43 considered themselves to be in good health", while 10 "considered their conditions fair". The authors qualify this statement by adding that, in the case of these last-mentioned patients, 9 complained of varying degrees of chest pain, including 2 who showed signs of possible chronic progressive histoplasmosis; nevertheless, 5 were on active military duty, and 3 were overseas.

The authors conclude from this experience that surgical intervention is justified in cases presenting with focalized pulmonary histoplasmosis, provided that the diagnosis of histoplasmosis is established.

C. J. La Touche

SWEANY, H. C. Histoplasmosis.

This book was reviewed on p. 104.

GARRETT, H. D. & ROBBINS, J. B. **An Unusual Occurrence of Sporotrichosis. Eight Cases in One Residence.** *Arch. Dermat.* 1960, Oct., v. 82, No. 4, 570-71.

"Eight cases of primary cutaneous sporotrichosis are reported, having occurred in individuals living and working in one residence in Juarez, Chihuahua, Mexico. The source of infection was proved to be *Sporotrichum schenckii* living on grass which was used in packing pottery for shipment from central Mexico to Juarez."

SÁENZ, G. F. Inoculación experimental de *Sporotrichum schenckii* en embrión de pollo. [Experimental Inoculation of *Sporotrichum schenckii* in the Chick Embryo] *Rev. Biología Trop.* San José, Costa Rica. 1960, July, v. 8, No. 1, 123-43, 26 figs. on 5 pls. [10 refs.]

The English summary appended to the paper is as follows:—

"Embryonated chicken eggs were inoculated with *Sporotrichum schenckii* by ten different routes: yolk sac, chorio-allantoic membrane, allantoic, extra-embryonic, and amniotic cavities, albumen sac, brain, muscle, blood vessels, and shell membrane. Five eggs were used in each type of inoculation. Detailed mycological studies and anatomo-pathologic microscopic examination were carried out, using P.A.S., Gram and hematoxylin-eosin techniques.

"The fungus behaved differently in the various tissues and fluids of the embryo. Pleomorphism was observed, including vegetative mycelium, reproductive mycelium, pseudomycelium, promycelium, blastospore production with one or several buds, small and large conidia, rounded and cigar-shaped cells. No asteroid formations were found."

MARPLES, Mary J. **Microbiological Studies in Western Samoa. II. The Isolation of Yeast-like Organisms from the Mouth, with a Note of Some Dermatophytes isolated from Lesions of Tinea Corporis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Mar., v. 54, No. 2, 166-70. [12 refs.]

As part of a microbiological survey in the human communities of Western Samoa [see this *Bulletin*, 1960, v. 3, 1112] the author studied the yeast-like flora of the mouth in some 251 subjects ranging from 3 to over 60 years.

Results showed yeast-like organisms in approximately 25% of the children and 40% of the adults. Two-thirds of the isolates were identified as *Candida albicans*. Of a total of 85 strains isolated, 58 were identified as *C. albicans*. Other species included: *C. parapsilosis*, *C. guilliermondi*, *C. tropicalis* and *C. krusei*.

It was found also that, as regards their capacity for production of chlamydospores, many strains behaved differently on different chlamydospore-promoting culture media: a feature which was noted previously by other authors. In fact a difference in the number of chlamydospores produced was exhibited even by subcultures of the same strain depending on whether they were grown in Dunedin or in Samoa.

It was found that the increased incidence of oral yeast-like organisms in adults as compared with their incidence in children bore no relation to the wearing of dentures; nor was it associated with the incidence of gingivitis or caries.

These results are compared by the author with her previous survey of the incidence of oral yeast-like organisms in university students and nurses in Dunedin, New Zealand, and with previous surveys of this nature by other workers.

This article also includes preliminary notes of the dermatophyte spectrum as observed so far in Western Samoa.

C. J. La Touche

ISENBERG, H. D., PISANO, M. A., CARITO, S. L. & BERKMAN, J. I. **Factors Leading to Overt Monilial Disease. I. Preliminary Studies of the Ecological Relationship between *Candida albicans* and Intestinal Bacteria.** *Antibiotics & Chemotherapy* New York. 1960, June, v. 10, No. 6, 353-63, 4 figs [31 refs.]

The problems concerning overt moniliasis associated with antibiotic therapy are not only of great importance but also of general interest. A wealth of literature contributed from many sources testifies to this. However despite the numerous investigations which have been carried out to elucidate these problems little practical information has emerged, perhaps because of the artificial conditions usually associated with *in vitro* experiments.

In an effort to gain further information on this subject under more natural but at the same time adequately controlled conditions, the authors of this article set themselves the task of studying the effect of bacterial populations on the behaviour of a strain of *Candida albicans* in culture.

The methods employed were various; thus, agar plates seeded with *C. albicans* were spot-inoculated with strain

of bacteria by the method of ROBBINS *et al.* (*J. Bact.*, 1957, v. 74, 377); such plates were also used for testing the action of bacterial culture filtrates on the growth of *C. albicans*; but the most interesting and significant method used was a dialysis assembly system. This apparatus, which consisted of the dialysis tube filled with culture fluid, itself immersed in culture fluid contained in an outer culture tube, was used for 2 distinct techniques, namely, the "successive cultivation technique" and the "simultaneous cultivation technique". The first of these consisted in inoculating the culture fluid inside the dialysis tube with a given bacterial species, withdrawing this tube after a period of incubation, then inoculating the culture fluid remaining in the outer culture tube with *C. albicans* and finally incubating this. Cell multiplication of the "yeast" was then calculated by an optical density method. The second technique consisted in inoculating the culture fluid inside the dialysis tube with a given bacterial species and also inoculating the culture fluid outside this with *C. albicans*, so that, on incubation, growth of the two organisms would be simultaneous.

Graphs representing results obtained by this dialysis method showed different degrees of stimulatory or inhibitory effect on the growth of *C. albicans* produced by a number of bacterial species, when the culture system was incubated in different atmospheres—aerobic, micro-aerophilic and anaerobic—with either the successive or the simultaneous method. One example of many must suffice to illustrate these effects. Thus, *Staphylococcus aureus* exerted a stimulatory effect on *C. albicans* which, when the simultaneous technique was used, was very marked under micro-aerophilic conditions, somewhat less under aerobic conditions, and still less under anaerobic conditions; whereas, when the successive technique was used stimulation by *Staph. aureus* was greatest under anaerobic conditions, less under micro-aerophilic conditions and least under aerobic conditions.

The most important conclusion to be drawn from these experiments is that atmospheric environment must be taken into account in assessing the inhibitory or stimulatory effects exerted by bacteria on the growth of *C. albicans*.

C. J. La Touche

WALKER, Leila, & HUPPERT, M., with the technical assistance of A. WOODS. **Corn Meal-Tween Agar: an Improved Medium for the Identification of *Candida albicans*.** *Amer. J. Clin. Path.* 1960, Feb., v. 33, No. 2, 190-94, 6 figs.

Following on previous investigations, the results of which were published by them [see this *Bulletin*, 1960, v. 35, 243], the authors compared the characteristics of mycelial growth of *Candida* species on corn meal agar, corn meal-Tween agar and rice-Tween agar.

Results showed that not only did all the cultures of *Candida albicans* produce abundant chlamydo-spores on corn meal-Tween agar and on rice-Tween agar, but so also did 4 of 5 cultures of *C. stellatoidea* and 5 of 8 cultures of *C. tropicalis*, while on plain corn meal agar *C. albicans* and *C. stellatoidea* produced relatively few chlamydo-spores. It was also shown that corn meal-Tween agar was superior to the other media for the production of characteristic mycelial growth in *C. albicans*.

C. J. La Touche

NEWTON, A., SHAW, E. D., GOODE, Claire S. & RIGGALL, Frances O. **Identification of *Candida albicans*. Further Work on the Rapid Identification of *Candida albicans*.** *J. Investigative Dermat.* 1960, Sept., v. 35, No. 3, 123.

"The results of this work indicate that sheep blood is superior to human blood when used in preparing blood agar for the culture of yeasts and yeast-like organisms in candle jars at 37°C. for 2 days. When cultured in this manner, *C. albicans* and *C. stellatoidea* are readily differentiated from other *Candida* species and other yeasts and yeast-like organisms by their ability to form distinctive filamentous-like colonies. This is a further aid in the rapid identification of *C. albicans*."

AKSOYCAN, N., LE MINOR, L. & LE MINOR, S. **Antigènes communs entre les *Candida* et les *Salmonella*-Arizona. [Existence of Antigens Common to *Candida* and *Salmonella* Arizona]** *Ann. Inst. Pasteur.* 1960, Nov., v. 99, No. 5, 723-8.

The English summary appended to the paper is as follows:—

"*Candida albicans*, *guilliermondi* and *tropicalis* are strongly agglutinated by anti-*Salmonella* 6,7 and 0,41 O-sera. Conversely, anti-*C. tropicalis* serum agglutinates suspensions of *Salmonella* 6,7, 6,8, 6,14,24,8, 20 and 41, anti-*C. guilliermondi* serum agglutinates 6,7 and 41 suspensions, anti-*C. albicans* serum, 6,7 and 8,20 suspensions. These three sera and anti-*C. stellatoidea* serum also agglutinate certain *Arizona* O suspensions.

"*C. krusei* and *C. parakrusei* did not show any antigenic relationship with *Salmonella*."

"Saturation tests show that these agglutinations seem to be due for the most part to minor antigens which are not mentioned in the antigenic tables used for the serologic diagnosis of *Salmonella* and *Arizona*."

HENDERSON, J. W., WELLMAN, W. E. & WEED, L. A. **Nocardiosis of the Eye: Report of Case.** *Proc. Staff Meetings Mayo Clinic.* 1960, Oct. 12, v. 35, No. 21, 614-18, 3 figs.

"The clinical course of a patient with an unusual granuloma on the surface of one eye is reported.

"The fungus, *Narcodia asteroides*, was cultured from specimens of this lesion.

"The patient was treated systemically with sulfadiazine and a topical application of sulfacetamide sodium.

"A very favourable response to treatment was noted."

GOWING, N. F. C. & HAMLIN, Iris M. E. **Tissue Reactions to *Aspergillus* in Cases of Hodgkin's Disease and Leukaemia.** *J. Clin. Path.* 1960, Sept., v. 13, No. 5, 396-413, 24 figs. (5 coloured). [48 refs.]

"Five cases of aspergillosis complicating Hodgkin's disease and leukaemia are reported. The organs involved were: lungs (all five cases), stomach (Case 3); brain and

meninges (Case 4); heart, kidneys, spleen, thyroid, and liver (Case 2). Cultures of *Aspergillus fumigatus* were obtained from the post-mortem tissues of three patients.

"All the lesions in Case 2 were suppurative. The other four cases had non-suppurative lesions characterized by spreading coagulation necrosis with peripheral hyperaemia, exudation, and haemorrhage. Invasion and occlusion of blood vessels occurred frequently.

"The various factors that may be responsible for the initiation and progression of the fungal infection are discussed. The available evidence suggests that *Aspergillus fumigatus* can produce toxic metabolites which are able to cause tissue necrosis and vascular damage. In patients suffering from neoplastic conditions of the lymphoreticular system, especially if steroid hormones or radiomimetic drugs are given, spreading, necrotizing lesions can develop unchecked by antibody or cellular defences."

MARSÁLEK, E., ŽIZKA, Z., ŘIHA, V., DUSEK, J. & DVORÁČEK, Č. Plicní aspergilóza s generalizací vyvolaná druhem *Aspergillus restrictus*. [Generalized Pulmonary Aspergillosis produced by *Aspergillus restrictus*] *Časopis Lékařů Českých*. Prague. 1960, Oct. 7, v. 99, No. 41, 1285-92, 14 figs. [27 refs.]

The English summary appended to the paper is as follows:—

"The authors present a report on pulmonary aspergillosis with subsequent generalisation.

"The causal agent was *Aspergillus* from the group *restrictus*, most probably *Aspergillus penicilloides* *spgazzini*.

"The authors describe the clinical course, the pathological findings and give a brief account of the properties of the isolated strain."

BELCHER, J. R. & PLUMMER, N. S. Surgery in Broncho-Pulmonary Aspergillosis. *Brit. J. Dis. Chest*. 1960, Oct., v. 54, No. 4, 335-41, 3 figs. on pl. [21 refs.]

SUTHERLAND, J. C. & JONES, T. H. Gastric Mucormycosis: Report of Case in a Swazi. *South African Med. J.* 1960, Feb. 20, v. 34, No. 8, 161-3, 2 figs. [15 refs.]

The case described by the authors of this article was that of a male Swazi aged about 50 years who was admitted to hospital "because of cough and blood-stained sputum and sharp pain in the chest which began 3 weeks previously." He also suffered occasionally from postprandial abdominal pain.

On admission, this patient was "weak and emaciated" and presented with a palpable epigastric tumour. He died on the 3rd day after admission.

At the autopsy, which was performed 48 hours after death, a greyish white tumour measuring about 3 by 2 inches was present along the greater curvature near the cardia. It was raised above the surface of the surrounding mucosa and was covered with a gelatinous exudate.

Further investigation revealed that this tumour was composed of "necrotic and haemorrhagic material which is diffusely infiltrated by numerous and non-septate hyphae typical of mucormycosis." Vascular invasion was also present.

There was no evidence of dissemination of the fungus.

Both lungs showed a "severe necrotizing pneumonitis". Therefore, despite the presence of the gastric lesion, it was considered that death was "probably caused by pneumonia".

[See also this *Bulletin*, 1957, v. 32, 446, 666.]

C. J. La Touche

BOSHES, L. D. A Review of Fungus Infections of the Central Nervous System. *Mycopathologia*. The Hague. 1960, Oct. 31, v. 13, No. 3, 215-36, 15 figs. [45 refs.]

CIFERRI, R. [Manual of Medical Mycology] Vol. II.

This book was reviewed on p. 101.

Communicable Diseases

The order in this section is:—Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

STEINBRÜCK, P. Schulkind und Tuberkulose. [Tuberculosis in Schoolchildren] *Ztschr. f. ärztl. Fortbildung*. 1960, Aug. 15, v. 54, No. 16, 932-4, 1 fig.

In 1949, 612 children aged 5-15 years died of tuberculosis in the East German Republic, but in 1958 only 16 died. In 1949 the rate of infectious tuberculosis was

4.9 per 10,000 children and of active non-infectious tuberculosis 101.8. The present rates are 1.06 and 39.5 respectively.

The decline in the incidence of non-pulmonary tuberculosis has been relatively smaller than that of pulmonary tuberculosis. It is only about one third less than the 1949 rate and the present incidence is higher in children than

in adults. Tuberculosis continues therefore to be an important factor in the morbidity of schoolchildren.

In 1954 6,289 schoolchildren (26.7 per 10,000) had tuberculosis but in 1958 the number fell to 2,652 (12.5 per 10,000). This decline will be accelerated in future because of the entry into the schools of larger numbers of children who have been vaccinated with BCG at birth.

The finding of a reactor rate of 20% in a survey made among school entrants indicates the need for the intensification of all available control and preventive measures. For example, many children in rural areas work in close contact with cattle, and with a bovine reactor rate of 50% it is clear that such children must often be exposed to tuberculous infection. There is room for improvement here, and a measure suggested is a ban on the employment of non-reactor children in close contact with cattle.

Steinbrück emphasizes the great value of BCG vaccination and quotes the disease rate in unvaccinated persons to be 15 times as high as in those vaccinated. He advocates that vaccination be made compulsory.

The value of mass radiography is stressed and its extension recommended. The annual X-ray examination of all adults who work in contact with children should be compulsory.

Tuberculous children should be treated with specific chemotherapy for a sufficiently long time, and adequate schooling should be provided especially for those with extra-pulmonary disease so that they may not fall behind other children. Specific treatment is advocated for children who have been infected recently as indicated by the tuberculin test.

H. G. Calwell

EL-MOHANDIS, M. N. & SAKR, R. **The Problem of Tuberculosis in Infants and Children in Egypt.** *J. Egyptian Med. Ass.* 1960, v. 43, 27th Arab Med. Congr. No., 99-118, 5 figs.

The available data concerning tuberculosis morbidity and mortality in Egypt are incomplete. Although notification has been compulsory since 1928 many doctors are reluctant to notify cases.

A mass BCG vaccination campaign was carried out in 1949-52 in the course of which the tuberculin reactor rate was found to be 6% at 0-1 year, 25% at 6-7 years and 47.8% at 13-14 years. A survey in a children's hospital in Cairo in the period 1951-59 gave rates of 2.7%, 20.1% and 61.2% respectively. These figures show clearly the high incidence of tuberculous infection in childhood.

During the period 1941-1951 the morbidity rate in out-patients at the same children's hospital was over 1%. More than 30,000 of the 2½ million children attending were found to have tuberculosis. In the same period 1,557 children were admitted to the hospital with tuberculosis. The death rate was 23.9% (52% at age 0-6 months and 13.6% at age 9-12 years).

The disease was pulmonary in 1,450 (93.4%) and extra-pulmonary in 107 (6.6%). There were 27 cases of meningitis (1.6%), 35 of peritonitis (2.3%) and 31 of disease of bones and joints (1.93%).

During the period 1951-59 21,750 children aged 0-15 years were tested with tuberculin. The reactor rate for the whole group was 17%. The rate was 2.7% at 0-1 year in both sexes and in those aged 12-15 years the reactor

rates were 55.8% and 66.2% in boys and girls respectively. The rate was higher in boys than in girls in the whole group; only after the 12th year was it higher in girls. It rose steeply after the 9th year.

X-ray examination of 3,866 reactors revealed tuberculous lesions in 618 (16.7%). It is noted that 17 children with proved tuberculosis failed to react to the Mantoux test with 100 TU of OT, of whom one was considered to have congenital tuberculosis.

The importance of contact with tuberculous persons was amply demonstrated. In a series of 109 newborn infants of known tuberculous mothers under treatment with chemotherapy conversion occurred in 36 (33%) of the infants in the first 3 months.

In another series of 27 infants separated from their tuberculous mothers at various intervals after birth none separated on the 2nd or 3rd days underwent conversion whereas conversion occurred in 1 of those separated on the 7th day after a period of 51 days and in 2 separated on the 10th day after 50 and 45 days respectively. The conversion rate in the series was 11.1%. As judged by the appearance of tuberculin sensitivity the incubation period would be from 40 to 58 days.

In view of the high reactor rate soon after the age of 9 the authors recommend that BCG vaccination should be done at a much younger age than this. "The [tuberculosis] problem [in Egypt] entails continuous efforts in epidemiological, medical and socio-economic spheres."

H. G. Calwell

MEYRUEY, M. H. **La tuberculose à El Goléa. [Tuberculosis in El Goléa, Sahara]** *Arch. Inst. Pasteur d'Algérie.* 1960, June, v. 38, No. 2, 138-50. [24 refs.]

El Goléa is an oasis in the Sahara and the centre of a desert region the area of which is 55,000 sq. kilometres. The population in December 1958 was 12,000 including 7,500 nomadic Chambaa, 3,000 Negroes and 1,500 of other races. Europeans numbered only 300.

The Nomads wander less than heretofore because of the disturbed state of the country on one hand and the attraction of regularly paid work with the oil companies on the other. There is much intermingling of different tribal groups. Agriculture and pastoral pursuits are giving way to industry, and social security is entering into the people's lives. This industrial revolution is the background to the tuberculosis survey reported here.

In 1958-59 more than 3,000 persons were tested by scarification with heat-killed BCG vaccine, and 2,489 returned for reading. The total reactor rate in Whites was 71.9% (58.9% at 1-15 years and 85% over 15). The total reactor rate in Negroes was 65.4% (43.5% at 0-15 and 87.4% over 15). The reactor rate in the whole group was 70.1% (54.3% and 86%).

It was seen that the total index of infection was somewhat higher in Whites than in Negroes, and the primary infection showed a predilection for 2 age groups viz. 2-6 years and 12-15 years. The rate was lower in young Negroes than in young white persons.

Comparison of these findings with those of earlier surveys [this *Bulletin*, 1940, v. 15, 220] led to the conclusion that tuberculous infection is becoming more frequent in the Sahara owing to the breaking down of

the isolation in which many communities were accustomed to live until recently.

Although X-ray examination was not available until 1957 there are many records of the types of tuberculosis encountered in the last 40 years. Both respiratory and non-respiratory disease was seen, and there is evidence that the white inhabitants were affected in greater numbers than the Negroes. Tuberculosis affects men and women equally but social conditions hinder women from being treated adequately. Infection within the family is of great importance.

In 1958 2,842 patients were examined by X-ray. No details of the findings are given but it is stated that the disease although severe often yielded quickly to specific treatment. Most of the patients with tuberculosis were aged 18-25 years. There was insufficient hospital accommodation and social and economic difficulties militated against the completion of the necessarily prolonged course of treatment.

The prevailing circumstances demand mass prophylactic action, and in the author's opinion this can only be achieved by BCG vaccination of all infants aged 3 months to 1 year by scarification without preliminary tuberculin testing. Revaccination should be done every 3 years until the age of 15 years. This is the method of FOLEY and PARROT [*ibid.*, 1954, v. 29, 602].

[See also *Trop. Dis. Bull.*, 1958, v. 55, 1182].

H. G. Calwell

KOCH, A. B. P. W. **Tuberculosis in Ghana.** *Tubercle*. 1960, Aug., v. 41, No. 4, 282-9, 1 map.

This article commences with a brief survey of the country and people generally, followed by a short account of the health services. A more detailed account is given of the extent of tuberculosis in Ghana and the services available for its control. In 1957 tuberculin testing on 7,400 persons of all ages revealed that 55% of the sample were tuberculin positive; and in the age-group up to 4 years positive reactions were found in more than 25%. The population of Ghana in 1957 was probably about 5 million. Judging from the samples of the population examined there are about 40,000 cases of active tuberculosis.

F. H. Young

DELORMAS, M. P. Orientation de la lutte antituberculeuse en Côte d'Ivoire. [**The Tuberculosis Campaign in the Ivory Coast**] *Méd. Afrique Noire*. Dakar. 1960, July 1-15, v. 7, No. 13, 281-2.

The author thinks that tuberculosis is not a new phenomenon in the Ivory Coast, but that there has recently been a rapid extension of the disease. More cases are now diagnosed than a few years ago, and in the towns the incidence, once overwhelmingly in the poor, is now increasing in those of better economic position; moreover, in the first 4 months of 1960, of 323 new patients, 28% were from Abidjan, 22% from other towns and 48% were from small villages, indicating serious rural incidence.

The author discusses diagnosis on a large scale, and control through BCG, isolation and chemoprophylaxis,

and recognizes the difficulty in ensuring correct use of drugs in the existing circumstances. A deliberate campaign of education through the formation of local committees is envisaged.

Charles Wilcocks

ISLAM, N., GIASUDDIN, M. & ISMAIL, M. **Tuberculosis Survey among Students of Dacca University.** *J. Trop. Med. & Hyg.* 1960, Sept., v. 63, No. 9, 206-8.

The City of Dacca in East Pakistan has a population of 600,000 and there is much overcrowding. The university has 3,000 students of whom 1,300 reside in hostels; these were selected for the tuberculosis survey described here because of convenience. An additional 345 students not living in the hostels asked to be included.

1,645 students were Mantoux tested with 1 and 10 TU of PPD. The percentage who reacted to 1 TU was 56.2 and to 10 TU 10.0. The total reactor rate was 66.3%.

All the 1,092 reactors were advised to have an X-ray examination but only 621 (56.8%) reported. Of these 55 (8.7%) had radiological evidence of pulmonary tuberculosis. Excluding the 471 absentees the discovery rate was 4.7%. 4 students with positive sputa were advised to discontinue their studies and have treatment. Those with negative sputa were allowed to continue ambulatory treatment from the hostel. [No information is given about the state of the disease discovered. Presumably it was active.]

The above findings suggest that if the incidence of tuberculosis in lower social groups is higher than in university students, which is probable, the official figure of tuberculosis morbidity in Pakistan is much lower than the reality. It should be considered as only about one-third to one-fourth of the actual morbidity. Extensive tuberculin and mass radiography surveys are called for.

H. G. Calwell

SULTAN, L., NYKA, W., MILLS, C., O'GRADY, F., WELLS, W. & RILEY, R. L. **Tuberculosis Disseminators. A Study of the Variability of Aerial Infectivity of Tuberculous Patients.** *Amer. Rev. Respiratory Dis.* 1960, Sept., v. 82, No. 3, 358-69, 2 figs. [19 refs.]

Since 1956 a quantitative study of air-borne infection has been in progress in an American hospital. The frequency of occurrence of tuberculous infection in guinea-pigs exposed to air exhausted from a 6-bed ward of patients with active pulmonary tuberculosis has been determined. The air exhausted through the ventilation system was passed through an animal exposure chamber. All patients had sputa positive for tubercle bacilli on direct examination. At the start and for 7 months the ward was mostly occupied by patients who had not responded to treatment. During the next 6 months previously untreated patients were used. While in the ward they received specific chemotherapy, and during this period the animal infections ceased. For that reason patients who were treatment failures were again admitted. Some of the patients with drug-resistant bacilli had organisms resistant to all of the drugs in use, while others were receiving drugs believed to be effective.

The results of 41 guineapig infections between November 1956 and April 1958 have been reported previously [this *Bulletin*, 1957, v. 32, 801]. Of these 41 infections 22 were cultured, and it was shown that 19 were due to 2 of a total of 62 patients. This paper adds the results until November 1958 which include 30 more infections, 26 of which were successfully cultured.

The time of residence of the patients, the time of infection of the guineapigs and the results of drug-resistance testing of the bacilli recovered from patients and animals were analysed in great detail. The bacteriological methods used are described.

The animal infections were divided into 9 groups, and it was believed that a single patient caused each group of these infections with the exception of one.

It was concluded that 35 of 48 cultured air-borne infections came from 3 patients even though 77 patients occupied the ward during the period of study. The reasons for the conclusion are stated.

The possibility of infection from sources other than the patients is discounted by the fact that when the exhausted air was irradiated animal infections ceased completely. Cross-infection between the animals was also discounted. The remarkable infectivity of the 3 patients may have been related to their ability to produce large numbers of bacilli unusually capable of withstanding the rigours of air-borne transmission. [See also *Ibid*, 1960, v. 35, 454.]

H. G. Calwell

GRIFFITH, A. H., BELLAMY, Marjorie J. & MCFARLANE, Jean K. **A Tuberculin Survey in a Large Urban Area.** *Tubercle*. 1960, Aug., v. 41, No. 4, 233-8.

A serial tuberculin testing programme was instituted in Cardiff (population 253,000) in 1958 with the object of detecting tuberculin conversion in children. It was the plan to offer tuberculin tests to all the children over 1 year of age. The Heaf test was used and read at 3-7 days.

There were 42,000 schoolchildren and 17,500 infants under the age of 5. The results of the tests were complete for 34,917 (83%) of the schoolchildren and 3,460 (20%) of the infants. Between 7 and 11% of the children aged 5-12 years had already been vaccinated with BCG and this had to be taken into account in assessing the rates of natural conversion.

The incidence of grade 3 and 4 (Heaf) reactions was lower in the vaccinated than in the natural reactors, 11% compared with 53%.

The results are tabulated according to age and degree of sensitivity. The table is too long to reproduce here but the totals were:

Previously vaccinated					
Grades of reaction					
Negative	Positive				Total
	1	2	3	4	
293	2,317	2,644	573	82	5,909

Unvaccinated					
Grades of reaction					
Negative	Positive				Total
	1	2	3	4	
29,625	778	551	907	607	32,468

The percentages of children of various ages infected naturally (after the exclusion of vaccinated reactors) increased from 0.9% at 1 year to 18.7% at 13 years.

X-ray examination was confined to children with Heaf reactions of grades 3 and 4. Their home contacts were also invited to attend for X-ray examination. Of 1,509 such children 1,214 were examined and 7 were found to have active pulmonary tuberculosis. 17 other children with inactive tuberculosis were advised to accept supervision.

1,011 adult contacts of the reactor children were X-rayed; 13 were found to have active tuberculosis. [It is not stated how often tuberculin testing of the non-reactor children is to be repeated in future.]

H. G. Calwell

KEEPING, J. A. & CRUICKSHANK, R. **Serial Tuberculin Testing of Young Children in a London Borough.** *Tubercle*. 1960, Aug., v. 41, No. 4, 239-46, 1 fig. [17 refs.]

In 1952 it was decided to investigate the tuberculin state of children living in the borough of Paddington, London, with the object of determining the rate of natural tuberculin conversion between the ages of 6 months and 5 years, the frequency of tuberculous disease following conversion, the value of detecting conversion as a pointer to tuberculosis in contacts and the relationship between types of tuberculous infection and known contact with an infector or environment.

The population which fell from 124,800 in 1952 to 115,700 in 1958 is mixed and contains many Irish, Poles, Austrians, Germans, Indians and West Indians; the number of the last rose from 291 in 1951 to 7,000 at the time of writing. Bad housing is common.

The jelly test was used without abrasion of the skin by flourpaper. The authors found it to be reliable, giving no false negative and only 0.5% false positive reactions when compared with the 10 TU Mantoux test. They concluded, however, that the Heaf test has advantages over the jelly test.

The plan was to test all children born in the period 1952-56 at intervals of 6 months between the ages of 6 months and 5 years. In fact only 4,833 children out of the 10,079 born entered the survey and persevered. The total number of tests was 13,179, an average of 2.7 per child in a period varying from 1½ to 4½ years. Children showing doubtful or positive jelly reactions were given a Mantoux test with 10 TU of OT. If the Mantoux test was positive the child was examined and X-rayed.

Of the 4,833 children 35 converted as follows—under 1 year, 0.02%; 1, 0.37%; 2, 0.74%; 3, 0.43%; and 4, 0.29%.

No clinical or radiographic evidence of tuberculosis was found in 16 (46%). There were primary intrathoracic lesions in 15, a suspected abdominal lesion in 1, phlyctenular conjunctivitis in 1, miliary disease in 1 and meningitis in 1.

8 new cases of adult tuberculosis were found for the 35 child reactors; in 13 more cases the child was in contact with a known infector although the contact was not necessarily recognized. Thus a source of infection was demonstrated in 21 (60%).

H. G. Calwell

FLECK, A. C., HILLEBOE, H. E. & SMITH, G. E., Jr.
**Evaluation of Tuberculosis Casefinding by Mass
 Small Film Radiography.** *Pub. Health Rep.*
 Wash. 1960, Sept., v. 75, No. 9, 805-13, 1 chart.

This paper presents the results of mass radiography surveys made in New York State in the period 1952-58. They included the general community and patients admitted to general hospitals; 96 of the 187 hospitals eligible to do so were participating in the scheme by the end of 1958.

A case of tuberculosis discovered in a mass survey was defined as one previously unreported and clinically diagnosed within 6 months after X-ray examination as active, probably active, reportable pleural effusion, or active extrapulmonary tuberculosis.

The discovery rate per 1,000 skiagrams fell steadily from 1.2 in 1952 (454 cases) to 0.4 in 1958 (187 cases), and the cost per case rose from 492 to 1,441 dollars. The greatest number examined was 522,914 in 1954 and the lowest number 388,012 in 1952.

The discovery rate was 0.5 in the general population, 0.5 in agricultural groups, 0.2 in schoolchildren and students, 0.4 in employees, 0.8 in patients admitted to large hospitals and 1.1 in those admitted to small hospitals. There was an association between the size of the population and the discovery rate, the rate being greater the greater degree of urbanization. This higher yield was not the result of greater survey activity in urban areas.

In the hospital series in 1958 the yield of new cases for males aged 15-24 was 0.2 per 1,000 and for males aged 25-34 it was 1.0. The rates in females were 0.1 and 0.3 respectively. This shows the greater value of examining persons over 25 years of age.

As a result of the above findings it has been decided to use mass radiography in New York State as follows.

Surveys of students, employees and residents of areas with less than 20,000 population will be discontinued. Surveys in areas of over 80,000 population will be intensified.

Contrary to the findings it has been decided to continue surveys at agricultural fairs because of valuable publicity and regardless of the yield of new cases. School teachers will continue to be included, regardless of higher cost, because of their special position in regard to the children in their care.

H. G. Calwell

WADDINGTON, J. K. B. **Surgical Aspects of the Mass
 X-Ray Campaign, Liverpool, 1959.** *Med. Officer.*
 1960, Nov. 11, v. 104, No. 20, 293-300, 3 figs.

During a mass radiography survey in Liverpool (population in 1957, 790,000) in 2 months of 1959, 205,713 males and 248,573 females over the age of 15 were examined by X-ray. The total represented 76.6% of the population over 15. The main object of the survey was the discovery of pulmonary tuberculosis but the author's interest was in patients likely to need surgical investigation (including bronchoscopy) and treatment.

235 patients were admitted to surgical wards of whom 58 (24%) were women. The lesions found were:

	Male	Female	Total
Mediastinal, neurogenic, diaphragmatic, chest wall and cardiovascular	10	14	24
Non-malignant pulmonary lesions subjected to operation	13	11	24
Active or inactive tuberculous lesions resected	9	4	13
Proved malignant pulmonary tumours	103	17	120
Suspected neoplasms, unproved	9	0	9
Non-malignant pulmonary lesions not needing surgery	33	12	45
	177	58	235

The most significant features of the carcinomas submitted to operation were the high proportion suitable for resection (90%), and the high rate of segmental resection or lobectomy (77%). Comparison of these rates with others reported shows that the lesions discovered by mass radiography were smaller and more localized than those discovered by routine methods. Most of the malignant lesions were found in the middle and lower social grades of the population.

In the cases of lung cancer which were proved conclusively a full analysis was made by age, symptoms and radiological findings.

Follow-up showed that 21 months after the start of the survey 31% of all patients who had pneumonectomy and 51% of those who had had pneumonectomy combined with segmental resection were alive and without signs of metastases or recurrence. No patient found to be inoperable at thoracotomy lived more than 15 months, and 75% of patients who were inoperable or refused treatment were dead.

H. G. Calwell

PUGSLEY, H. E., ALLEN, E. A., CHEUNG, O. T., COULT-HARD, H. S. & GALE, G. L. **Results of the Treatment of Tuberculosis before and since the Introduction of Chemotherapy.** *Canadian Med. Ass. J.* 1960, Aug. 27, v. 83, No. 9, 424-9. [11 refs.]

This paper sets out to compare the results before and after the introduction of chemotherapy in cases of active pulmonary tuberculosis. The definitions used are those of the National Tuberculosis Association. The observation period of the cases treated by drug therapy in this paper is 5 years. The reports from the Trudeau Sanatorium and the Herman Biggs Hospital show that before chemotherapy was introduced, in minimal cases the expectation of death in 10-20 years was 5%, in moderately advanced 20%, and far advanced 70% of the patients. At the Toronto Hospital starting in 1953, 140 patients were treated and followed for 5 years, the mortality for minimal and moderately advanced cases was nil, and for far advanced cases 11%. The average duration of triple drug therapy given to the patients was 17 months. Such results cannot be expected if the period of administration of the drugs is not adequate. Most of the patients ceased

to have a positive sputum within 6 months and all were sputum negative in 18 months. In patients treated for an average of 17 months (140 patients) at the end of 3 years, 100% of the minimal, 97% of the moderately advanced and 81% of the far advanced had achieved inactivity. The relapse rate of patients followed up for 2-5 years was 4%, compared with 30% in a Memphis hospital before the introduction of drug therapy. Treatment by resection was necessary in 22% of the series.

The Veterans Administration of the United States reported on 114 patients with pleural effusion: by the end of 5 years 4% of those treated with drugs had developed tuberculous complications compared with 23% in those treated before chemotherapy was introduced. In 33 patients suffering from bone and joint tuberculosis the tuberculous mortality was nil in those treated with drugs as against 27.5% in 58 cases before the treatment with drugs. 163 patients suffering from adequately treated renal tuberculosis had a tuberculous mortality of 1%, against a mortality of 46% in those not treated with drugs (period 1931-47). Meningeal tuberculosis, previously almost invariably fatal, showed a survival rate of up to 78%.

This paper confirms in statistical form the known revolution in prognosis produced by drug therapy.

F. H. Young

ROQUE, F. T. **A New Face of Tuberculosis.** *Amer. J. Med. Sci.* 1960, July, v. 240, No. 1, 17-20, 6 figs.

This paper gives details of 4 cases of acute pulmonary tuberculosis in which very rapid radiological clearing took place under treatment with large doses of isoniazid (together with PAS or streptomycin or both). In 3 patients practically complete clearing had occurred in 4-6 weeks; in 1 patient there was a definite cavity (2.5 cm.). Tubercle bacilli were recovered from 2 patients, and in the other 2 the clinical and radiological picture was typical. The author reports these cases to show that the diagnosis of pulmonary tuberculosis should not be discarded because very rapid clearing of the lung and the X-ray picture has taken place.

F. H. Young

HUTTON, P. W. & TONKIN, Isabel M. **Ethionamide ('1314') with Streptomycin in Acute Tuberculosis of Recent Origin in Uganda Africans: a Pilot Study.** *Tubercle.* 1960, Aug., v. 41, No. 4, 253-6.

Streptomycin was given in a daily dose of 1 gm. intramuscularly, 1 gm. of ethionamide was given in 4 divided doses by mouth, the full daily dose of 1 gm. being attained by slowly increasing the dose during the first week. The 7 patients were treated in bed. 3 had extensive, 2 moderate, and 2 slight cavitation; shadowing was present in 5 zones in 4 patients, and 4 zones in 3. At the end of 6 months 3 patients showed considerable, 4 moderate, radiographic improvement. None deteriorated. Cavities had disappeared in 3 patients, become smaller in 3, in 1 patient the cavity was larger. At the start of treatment all patients had direct positive smears, and all had probably positive cultures. In all cases the bacilli were sensitive to the standard drugs and ethionamide. At the

end of 5 months all 7 cultures were negative. At the end of 6 months 1 culture grew a single colony of tubercle bacilli. This was resistant to all drugs. Direct smears from this patient were persistently positive throughout 5 months of treatment, but unfortunately he was lost sight of. No patient had to discontinue treatment owing to nausea and vomiting. Gynaecomastia occurred in 3 patients, in 2 of whom it was troublesome.

The results are compared with those obtained in the Medical Research trial on streptomycin alone. It is considered that the combination which was tried gave results considerably superior to those reported with streptomycin alone. The authors consider that their figures suggest that ethionamide may have an action in preventing the emergence of streptomycin-resistant strains, and that a large controlled trial is needed so that their results may be confirmed.

F. H. Young

KRZYSKI, T. K. & YOUNG, R. C. **Hypersensitivity to Para-Aminosalicylic Acid.** *Canadian Med. Ass. J.* 1960, Sept. 3, v. 83, No. 10, 527-30. [11 refs.]

Over a period of 5 years hypersensitive reactions to PAS were found in 33 patients out of 894 (3.6%) who received treatment with PAS at the Prince Edward Hospital, Sydney, Nova Scotia. The dosage varied from 6 to 12 gm. of PAS each day. A table of the type and number of reactions is given, skin eruptions occurring in 24, fever in 21, gastro-intestinal in 6, and oedema of the eyelid and face in 6. Other forms of reaction occurred in small numbers. Hepatotoxicity occurred in 2 patients only; the authors consider that this small number was due to the fact that they discontinued the drugs after the first manifestation of reaction. They consider that the deaths reported from this are probably due to the fact that the treatment was continued too long. There were no deaths and all made good recoveries after the drug was stopped. 4 cases are reported, showing particularly interesting features. A general discussion referring to the literature on the subject follows.

F. H. Young

BELL, W. J. & BROWN, P. P. **Bacterial Resistance to Streptomycin, PAS and Isoniazid in Untreated Patients with Symptomatic Pulmonary Tuberculosis in Ashanti.** *Tubercle.* 1960, Aug., v. 41, No. 4, 247-52. [20 refs.]

This paper, from Ghana, deals with the bacterial resistance to standard drugs found in 448 specimens of sputum collected from all patients with previously untreated pulmonary tuberculosis presenting for treatment between May and December 1958. The methods adopted are detailed.

Of the 448 specimens of sputum, 343 were positive on culture (76.6% of the total). Of these 275 (80.2%) were sensitive to all drugs. 53 (15.4%) showed some degree of resistance. 87.5% were fully sensitive to streptomycin, 2% partially resistant, and 6.2% fully resistant. 90.4% were fully sensitive to PAS, 4.1% partially resistant, and 1.2% fully resistant. 86.9% were fully sensitive to isoniazid, 3.5% partially resistant, and 5.3% fully resistant.

The causes of this high incidence of resistance are

discussed. It was thought that family contact was a considerable factor in the spread of drug-resistant organisms, as many of the subjects with resistant organisms were friends or relatives of patients already receiving treatment at home, and living with them in close insanitary conditions.

Preliminary estimates suggest that 37.6% of those who acknowledged that they had had previous chemotherapy had cultures resistant to streptomycin, 28.6% to isoniazid and 4.8% to PAS. Where resistance was demonstrated in previously untreated cases, no less than 11% were resistant, or partially resistant, to all 3 drugs. Taking the experience in East Africa [this *Bulletin*, 1960, v. 35, 663] as a criterion, the authors fear that this percentage will steadily rise.

F. H. Young

KRAAN, J. K. & VAN DIJK, B. De toepassing van 1314Th en kanamycine bij patiënten met longtuberculose. [The Use of 1314Th and Kanamycin in Patients with Pulmonary Tuberculosis] *Nederl. Tijdschr. v. Geneesk.* 1960, Aug. 27, v. 104, No. 35, 1658-63, 7 figs. [16 refs.]

The authors have investigated the use of kanamycin and 1314Th (α -ethylisonicotinic acid thioamide) [this *Bulletin*, 1959, v. 34, 621] in the treatment of 8 patients suffering from pulmonary tuberculosis, 6 of whom had been treated with usual drugs and were infected with resistant organisms. Each patient initially received 250 mgm. of 1314Th per day, which was raised to 750 mgm. over a period of 7-10 days. Thereafter 0.5 gm. of kanamycin was given daily in addition. 7 patients had cavitation in the lungs and 6 had sputum containing *Mycobacterium tuberculosis*. The period of treatment varied from 3 to 10 months and averaged 5 months. 3 case histories are given in detail and the radiological findings are illustrated. In all cases the condition of the patients improved, as shown by diminution in size of the cavities, and in 2 patients complete healing of the cavities occurred. The sputum remained positive in only 1 case. During treatment 3 patients had anorexia and nausea.

Anne Tothill

ALBRECHTSEN, S. & WINSLOW, J. Corticosteroidbehandeling ved lungetuberculose. [Corticosteroid Therapy for Pulmonary Tuberculosis] *Nordisk Med.* 1960, Nov. 3, v. 64, No. 44, 1384-7, 2 figs. [17 refs.]

The English summary appended to the paper is as follows:—

"An account is given of 18 patients with pulmonary tuberculosis, who from the spring of 1955 up to January 1959 were treated with corticosteroids and by chemotherapy.

"All of them had bilateral pulmonary tuberculosis and the indications for treatment was in every case the patient's poor general condition.

"In 11 cases prompt and marked improvement was noted both subjectively and objectively.

"In no case was the tuberculosis aggravated by corticosteroid therapy."

ROYAL NETHERLANDS TUBERCULOSIS ASS. **Rehabilitation of the Tuberculous in the Netherlands.** 30 pp., 1 diagram. [? 1960.] The Hague: 7, Riouwstraat, Holland.

The definition of rehabilitation given here is "a complex of measures of a medical, socio-medical and social character which have as their ultimate aim and object the preservation and strengthening of the healing that has been achieved, and the ex-patients' re-employment as a fully able person in the industrial labour-process".

The principal reason why rehabilitation is essential for a patient with healed tuberculosis is the tendency of the disease to relapse. 15-20% of such patients appear to relapse within the first 5 years of being classified as recovered. Some patients relapse after that period. It is therefore essential to keep all cured patients under prolonged and regular supervision. This is the work of the tuberculosis clinics.

There is evidence that the frequency of relapse is decreasing but although resumption of work has often no clear influence on the occurrence of relapse there are occupations where unfavourable influences are present, and care should be taken in judging the suitability of an occupation for an ex-patient. The chest physician should consult with a vocational adviser or an industrial medical officer in such matters.

In the Netherlands every compulsorily insured worker is entitled to sickness benefit of 80% of his wages for 1 year, and some industries add a supplement of 20% in chronic illness. The maximum benefit is extended by another 2 years in case of tuberculosis if the patient is married or a bread-winner, his tuberculosis is curable, he follows the course of treatment prescribed and is under the age of 65. [This is very generous by United Kingdom standards but the report draws attention to its inadequacy for the unmarried, dependent tuberculous person.] If the disease is due to occupation or has been contracted from a fellow-worker free medical treatment is provided in addition to sickness benefit. [Are other tuberculous patients not treated free?]

On recovery the allowance continues during unemployment, and training, re-training and occupational resettlement courses are available. In many sanatoria training starts before discharge but in most cases the work is not, or is only partly, adapted to the patient's future occupation.

More than 80% of patients with healed tuberculosis in the Netherlands are re-employed within 3 months of being declared fit for work. The minority are principally unskilled workers of whom only 50% find employment within 3 months. About 85% of the re-employed find work in an equivalent job to the one they had before their illness.

H. G. Calwell

GRIFFITHS, Margaret I. **Multiple-Puncture Vaccination in the Newborn with Freeze-Dried B.C.G. Vaccine.** *Brit. Med. J.* 1960, Oct. 15, 1116-19, 1 graph. [12 refs.]

If intradermal BCG vaccination by injection is to be free from such complications as local or gland abscess it must be done with a high degree of skill. A reliable

method of inoculation requiring less skill would clearly offer great advantages especially in the under-developed countries where the need for BCG is as great as the supply of skilled personnel is small.

With this in mind an investigation of multiple-puncture vaccination of newborn infants was undertaken by using freeze-dried BCG vaccine. Since March 1958, 2,221 babies have been vaccinated thus in Manchester. No complications occurred.

Concentrations of 125, 83 and 50 mgm./ml. were used. At the beginning an ordinary Heaf tuberculin gun was used, and by rotating it 12 punctures could be made. Later other guns were designed to make 20 punctures at 1, 2 or 3 mm. penetration.

The effect of the number of punctures on post-vaccinal tuberculin sensitivity to 100 TU at 4 weeks and 10 TU at 1 year was examined. It was seen that sensitivity produced at 4 weeks and persisting at 1 year gradually improved as the number of punctures increased and that the depth of penetration was more important than the number of punctures. It was concluded that 20 punctures at 2 mm. will produce adequate tuberculin sensitivity in the newborn.

The results of varying the concentrations of the vaccine were examined. Increase above 50 mgm./ml. did not increase the degree of tuberculin sensitivity at 4 weeks but vaccine of 83 mgm./ml. was easier to use because it was more viscous and did not run off the arm so readily.

Later types of guns were tried, and it was found that a type with needles of greater diameter and shorter bevel produced a stronger tuberculin sensitivity at 4 weeks.

Comparison with the results of intradermal vaccination showed that the method of multiple-puncture vaccination used was just as effective.

H. G. Calwell

IRVINE, K. N. & BARR, A. **Observations on Vaccinating Schoolchildren with Danish Fresh B.C.G.** *Brit. Med. J.* 1960, Oct. 15, 1119-21.

During the school year 1956-57 8,990 English children aged 13 years were vaccinated intracutaneously with fresh Danish BCG vaccine (0.75 mgm./ml.). None of the children was in contact with a known tuberculous infector at the time of vaccination.

The pre- and post-vaccinal tests were the Mantoux with 10 TU of PPD in 5,390 children and the Heaf test with PPD in 3,600. Both tests were read at 2-4 days; the criterion of a positive Mantoux reaction was induration of 6 mm. or more and of a Heaf reaction induration at 4 punctures. Only non-reactors were vaccinated.

The post-vaccinal Mantoux tests fell by chance between 7 and 18 weeks and the Heaf tests between 6 and 19 weeks. The overall Mantoux conversion rate was 96.8% and the Heaf rate 97.7%.

In the Mantoux series the conversion rate between 7 and 18 weeks remained within the range of 93.7-100%, and did not decline or increase. In the Heaf series the conversion rate rose from 94.1% at 6 weeks to 99-100% at 11-19 weeks. However, 96 of the children tested at 6-11 weeks had no vaccination lesion, and if all such are excluded the overall conversion rate in the Heaf series shows no upward or downward trend.

The average diameter of the vaccination lesion did not

vary by more than 3 mm. in either series, which allows valid comparison between its size and the conversion rate to either test. Only 0.4% of children with vaccination lesions failed to become tuberculin sensitive, and there was found to be an association between the diameter of the vaccination papule and the degree of post-vaccinal tuberculin sensitivity. The authors emphasize that this relationship is shown only for the potent fresh Danish vaccine used.

The conclusion is that the presence of any local reaction to Danish fresh vaccine indicates successful vaccination. Only persons with no local reaction to vaccination require a post-vaccinal tuberculin test.

H. G. Calwell

VOJTEK, V. **The Incidence of Tuberculous Meningitis as an Indicator of the Efficacy of BCG Vaccination.** *Tubercle.* 1960, Aug., v. 41, No. 4, 272-5.

The object of this investigation was to examine the effect of mass BCG vaccination of the newborn on the incidence of tuberculous meningitis in Czechoslovakia. The author points out that the trial was not statistically controlled and that there may have been bias in the exposure of the two groups (vaccinated and non-vaccinated) to tuberculosis.

Compulsory BCG vaccination was introduced in Czechoslovakia in 1953 and an exact system of notification of tuberculous meningitis was introduced in 1954.

In the period 1954-58 793,976 children were born in Czech regions, of whom 753,138 (94.9%) were vaccinated with BCG in the first 10 days of life. The corresponding figures in the Slovak region were 487,665 of whom 415,904 (85.3%) were vaccinated. Infants with congenital abnormalities, eczema or weighing less than 2,500 gm. are not vaccinated. Inability to segregate an infant from an infector is not regarded as a contra-indication to vaccination. Although vaccination is compulsory it has not always been done if parents objected.

Because of different tuberculosis morbidity rates and the difference in the proportion of infants vaccinated in the 2 regions the changes in notification of meningitis are tabulated separately for each. The tuberculosis morbidity rate was consistently much higher in Slovak than in Czech regions.

In the Czech regions the notifications of tuberculosis meningitis averaged 0.8 per 100,000 births among the vaccinated and 10.9 among the unvaccinated. The rate in the unvaccinated was 13.5 times that in the vaccinated. The rates in the Slovak regions were 3.5 and 53.9 respectively. The meningitis rate among the unvaccinated was 15.3 times that in the vaccinated.

In 1954 there were 310 notifications of tuberculous meningitis in children under 15; in 1958 there were 100.

H. G. Calwell

BIRKHÄUSER, H. **Tuberkulosebekämpfung in der Schweiz—wohin? [The Campaign against Tuberculosis in Switzerland—the Future?]** *Schweiz. med. Woch.* 1960, Oct. 1, v. 90, No. 40, 1124-6.

Notification of cases of tuberculosis is the basis of efficient prevention. In Switzerland, however, infectious

tuberculosis is only notifiable whenever the doctor thinks that there is danger to the patient's contacts. Information about the incidence of the disease is therefore very incomplete.

On the other hand Denmark has had compulsory notification of all cases of pulmonary tuberculosis whether bacillary or not since 1905, and non-pulmonary tuberculosis has been notifiable since 1951. The death rate from tuberculosis in Denmark is the lowest in the world, and the morbidity rate is one of the lowest.

Both in Denmark and Holland there are regular mass surveys including especially tuberculin surveys in young persons, and even with an increasingly favourable tuberculosis situation there has been no relaxation in efforts to control the disease. In Denmark there are 2-3 per 10,000 new cases annually which, in terms of the population of Switzerland would mean 1,000-1,500 new cases annually. The actual figures for Switzerland are about 3 times higher.

It is most important to keep under observation certain classes of persons after a mass radiography survey. It is true that the greatest absolute number of new cases of tuberculosis will occur among those with previously

normal skiagrams (Danish figure 0.27 per 1,000), but the rate in the group with lesions classified as inactive is 0.51 per 1,000. Fibrotic lesions have been shown to be the least stable.

It was concluded in Denmark and Holland that all persons found to have tuberculous pulmonary infiltrates should be kept under prolonged observation but repeated annual X-ray examinations of adults with normal skiagrams are not worth while. Non-reactor children do not require routine X-ray examination.

In spite of the eradication of bovine and good control of human tuberculous infection in Denmark 20% of young persons aged 20 years are tuberculin reactors. The comparable rate in Swiss army recruits is 40-50%. Hypersensitivity to the Mantoux test with 10 TU at the age of 15-24 is a danger sign. Primary infection of young persons is much more dangerous after the age of 12 years than before it.

The conclusion from the above is that if Denmark with its low tuberculosis mortality and morbidity rates continues to pursue a full programme of control and prevention, Switzerland with a less favourable record cannot afford not to do likewise. *H. G. Calwell.*

VENEREAL DISEASES

ZTSCHR. F. ÄRZTL. FORTBILDUNG. 1960, Sept. 1, v. 54, Nos. 17/18, 972-1038, 17 figs. [Numerous refs.] [Papers on Venereal Diseases.]

The 17 papers assembled here give a picture of the present trends of venereal disease in East Germany from the viewpoints of diagnosis and treatment and seen as an individual and community problem.

The modern treatment of syphilis is described from experience in Leipzig (W. GERTLER, pp. 972-977) where since 1954 penicillin has been used almost exclusively with excellent results. The scheme of treatment and its success are fully stated. Other antibiotics have been used occasionally in certain circumstances.

There are several papers on diagnosis, in 1 of which the author (Albrecht KERN pp. 984-989) discusses the question of whether it is still desirable to carry out the classical serological tests. In Germany it is enjoined that every serum specimen should be examined by a complement-fixation test and at least 2 flocculation reactions. Since the introduction of the Nelson test in 1949 diagnosis can become more precise; nevertheless the new test has certain shortcomings. Tables set out in some detail the serological reactions which are available to obtain an optimal serological picture; the diseases in which false positive test reactions may occur; and the frequency of such false positives with different tests. The main conclusion is that the selected and improved classical serological tests are still essential in spite of the undoubted value of the Nelson test.

The Nelson test is considered in 2 other papers in which very guarded opinions are expressed. The technique is very complicated; the results of the test on the same

serum carried out at different laboratories has given widely different answers and it has been found unsuitable in some stages of syphilis.

Difficulties in the microscopic diagnosis of gonorrhoea are described in a short paper and these are due in the main to the increased incidence of diplococcal infections in the last years.

The legal measures for the control of venereal disease in the East German Republic are considered (Dieter HÖRIG, pp. 978-984) with a long detailed account and discussion of a new enactment which is soon to come into force for the prevention and control of such disease. It contains provisions for the examination and treatment by authorized doctors only, notification, prevention by spread of infected persons, the education and duties of patients and the follow-up of cases. It is believed that this new legal measure will prove to be effective.

The same author also contributes a long and interesting paper (pp. 1001-1011) on the experience of venereal disease in Dresden with consideration of the associated social hygienic problems. After World War II there was a catastrophic increase in the incidence of venereal disease and there is a description of the measures adopted to ascertain the extent of this increase and to combat the infections. Figures and graphs set out the statistics for 1950-59, admittedly minimum figures, which are analysed by sex and age. The difficulties of finding the source of infection are fully described. There is also an interesting account of the approach to the problems of prostitution and promiscuity with a comparison of this approach in a socialist state with that of the capitalist state of Western Germany.

There are several other papers on venereal disease and

its social problems. In 1 of these there is much statistical information on infected persons and the problem of promiscuity. The author states the opinion that in East Germany, where socialism is developing, the new ethic, which is distinct from that of capitalism, has much greater potential for development and this will inevitably lead to a better relationship between the sexes.

In an interesting paper on the psychology and neurotic reactions of persons with venereal disease (G. DESTUNIS pp. 992-996) the author deals with such subjects as the family conflicts which may arise if a person acquires the disease; the nature of those who are infected which in general is that they are emotionally, sexually and socially immature though physically and mentally mature; psychopathic features of prostitutes; the behaviour of girls designated as HwG-persons ["pick-ups", see, WITTKOWER, this *Bulletin*, 1948, v. 23, 769, to whom the author refers] and neuroses or other psychic disorders which may result from venereal disease.

The prophylaxis of venereal diseases is considered in a short paper (H. HERING pp. 1026-29). The author discusses mechanical and chemical methods of prevention, the dangers of attempts at self-sanitation by the person at risk and official procedures that have been adopted in armies. The prevention of congenital syphilis and of infection from the blood of donors is also mentioned.

Included in this assembly of papers is one on problems of sterility and impotence in the male. There is an account of the information which is to be obtained when the patient comes for investigation and advice but most of the paper is devoted to the technique of sperm examination, the assessment of the results of this and the possibility of treatment.

M. E. Delafield

LOEB, M. B. **Future Problems of Venereal Disease Control affected by Increased Teenage Population.** *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 191-3.

The teenage population will represent 17% of the whole in the United States in 1960 and is likely to rise even further; the increase is not only relative but absolute and the trend is for teenagers to concentrate in coastal urban centres; sexual activity among adolescents will increase. Venereal disease is likely to be increased by indiscriminately promiscuous girls who are emotionally sick. With increase of teenagers more boys will have access to those girls. Preventive measures include (1) health education by relatively non-authoritarian adults who will listen and discuss rather than by priest, parent and physician; (2) provision of opportunities for the teenage boy to express his masculinity in appropriate ways; (3) improved mental health services in schools to help those who are mentally disturbed and to provide psychiatric care.

[Not everyone will agree with all the opinions expressed in this article, for instance: Sexual activity among adolescents will increase. It is possible that this will lead to a greater increase in illegitimacy and in early marriages rather than an increase in venereal disease. The girl quoted who had sexual relations with 15 boys and infected 9 of them with gonorrhoea is an example of the contrary opinion.]

T. E. Osmond

HARRIS, A., BOSSAK, H. M., DEACON, W. E. & BUNCH, W. L., Jr. **Comparison of the Fluorescent Treponemal Antibody Test with other Tests for Syphilis on Cerebrospinal Fluids.** *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 178-80.

These authors tested 428 cerebrospinal fluids in parallel using the fluorescent treponemal antibody (FTA), TPI, KRP (Kolmer complement fixation test with Reiter protein antigen) and VDRL tests; 59 fluids were from persons about to submit to spinal anaesthesia and 369 were from treated (penicillin) syphilitic subjects. The FTA gave 82, TPI 18, KRP 12 and VDRL 16 positive reactions; all 4 tests agreed in 350 (82%) and in 52 the FTA alone was positive.

When quantitative reactions were carried out with FTA, titres ranged from 1/1 to 1/640 (mean 1/35). Two of the pre-anaesthesia patients were positive with FTA only; one was syphilitic and the other possibly so. Table I gives comparative test reactivities on all specimens and Table II quantitative FTA results in each of the 2 series.

[These results do not tell us very much except the relative sensitivities of the 4 tests; presumably most of the 59 were non-syphilitic and many of the 369 may be supposed to have been cured or at least not to have suffered from central nervous syphilis. The great preponderance of positive FTA reactions over the other 3 tests, 2 of which are well established, suggests that the FTA is over-sensitive; it would be interesting to know the results of the 4 tests on the 57 presumably non-syphilitic cerebrospinal fluids.]

T. E. Osmond

MONTGOMERY, C. H., SUHRLAND, Sylvia & KNOX, J. M. **Observations concerning Fluorescent Treponemal Antibody Test for Syphilis.** *J. Investigative Dermat.* 1960, Aug., v. 35, No. 2, 95-101, 1 fig.

This test (FTA) was carried out in parallel with VDRL and RPCF on sera from various stages of syphilis. In primary syphilis FTA was reactive in 19-23% where both the others were non-reactive: all 3 tests agreed (positive and negative) in 65-39%. In secondary syphilis 14 out of 15 sera were positive with all tests and 1 was negative with RPCF only; similar results were found in early latent cases; in 14 late latent cases FTA and RPCF were each negative, in 2 cases, all the rest being positive. For all stages of syphilis the reactivity percentages were: FTA 92, VDRL 85 and RPCF 80; in 60 specimens from normal persons all tests were negative. When quantitative tests were carried out FTA consistently showed much higher titres than VDRL.

As regards the effects of treatment, in primary cases FTA and VDRL both showed a fall in titre in 8 out of 11 patients and 5 became non-reactive; in secondary cases 4 out of 7 showed a fall and 2 showed higher titres; of 15 early latent cases 10 showed reduced titres (2 became non-reactive), in 2 there was no change and in 3 titres rose.

It is concluded that FTA detects a different antibody from TPI, or is more sensitive, and that this antibody is similar to reagin and therefore is not responsible for the immunity found in late syphilis.

T. E. Osmond

EL GHOROURY, A. A. A. **Comparative Performance of Four Serological Tests for Syphilis on Sera from Lepers and Tuberculous Patients.** *J. Egyptian Pub. Health Ass.* 1960, v. 35, No. 2, 63-80. [15 refs.]

Sera from patients in Alexandria suffering from leprosy and tuberculosis are known to give some positive reactions with routine serum tests for syphilis. This author submitted 376 sera from male leprosy patients and 220 from tuberculous patients to 4 tests, viz. Meinicke, Kolmer and Kahn with lipoidal antigen and VDRL with cardiolipin antigen. The following were the percentages of positive and doubtful reactions: Meinicke 9.5, Kolmer 14.7, Kahn 18.8 and VDRL 19.0; figures for the sum of reactions with 2 tests were Meinicke-Kolmer 18.4, Meinicke-Kahn 20.3, Meinicke-VDRL 21.9, Kahn-Kolmer 23.9, VDRL-Kolmer 24.6, and Kahn-VDRL 25.3. Only 10 out of 279 leprosy sera and 4 out of 214 tuberculosis sera were reactive with all 4 tests.

162 sera were sent to the WHO Serological Reference Centre in Copenhagen for comparison of the results with Kahn and VDRL tests; results showed Kahn reactive in 10.5% in Copenhagen and 26.3% in Egypt; corresponding figures for VDRL were 11.8% and 25.1%.

Sera were more often positive in lepromatous than in neural cases and tended to decrease with duration of the disease but reactions tended to increase in tuberculosis.

Detailed results, many of which are of no great interest, are set out in 7 tables. Results obtained by a number of other workers are given and compared with those of the author.

It is concluded that Meinicke is the most specific of the 4 reactions [but since patients with leprosy are known to be not infrequently infected with syphilis some of the figures given must be accepted with reserve].

T. E. Osmond

ENG, J. & JENSEN, R. A. Serologiske erfaringer ved rutinemessig undersøkelse av norske sjøfolk med *Treponema pallidum* Immobilization Test (TPI). [Serological Results of Routine Examination of Norwegian Seamen by the *Treponema pallidum* Immobilization Test (TPI)] *Nordisk Med.* 1960, Oct. 13, v. 64, No. 41, 1285-8. [13 refs.]

The English summary appended to the paper is as follows:—

"In Norway, all seamen are subjected to medical examination, including serological syphilis testing, when signing on. A series of 5,383 seamen is presented, in which the TPI-test was carried out on all sera which gave positive reactions with one or more of the standard tests employed. These were Meinicke's clarification test II (MKR), Bordet-Wassermann's complement-fixation test (WaR) and a flocculation test (Wadsworth & Brown's test or the VDRL-test).

"Of 102 seamen who gave positive reactions with the MKR or the WaR or both, 92 were TPI-positive. Out of the 10 TPI-negative ones, 2 had been treated for early syphilis 23 years previously. Similar observations are reviewed from the literature, and their practical consequences pointed out, namely: 1) A patient showing posi-

tive standard tests and a negative TPI-test should not be regarded as a false positive reactor unless physical examination and the case history have failed to reveal evidence of late syphilis, i.e. the evaluation should not be based solely upon a negative TPI-test and the exclusion of primary syphilis; 2) the sensitivity of the TPI-technique should be kept as high as possible; 3) it is unwise to replace the TPI-test by less sensitive treponemal tests.

"The frequency of seropositive syphilis in the series was 2.20 per cent, which is many times the frequency in the Norwegian population as a whole.

"The frequency of non-specific reactors in the present series is compared with that in a group of pregnant women, recently examined in exactly the same manner. The relative frequency of non-specific reactors in the MKR/WaR-tests was 7.84 per cent among the seamen, but 18.63 per cent among the pregnant women, in accordance with the far lower frequency of seropositive syphilis among the pregnant women (0.37 per cent). The absolute frequency of non-specific reactors to the MKR/WaR-test was 0.154 per cent among the seamen and 0.078 per cent among the pregnant women; this fact constitutes strong evidence that pregnancy per se is not a cause of false positive reactions in these two standard tests when carried out with the techniques which are employed in this laboratory."

WILLCOX, R. R. **Influence of Methyl Prednisolone on the Outcome of the Treatment of Acute Gonorrhoea in the Male with Tetracycline.** *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 187-90.

Steroids have anti-inflammatory properties and it was thought they might facilitate the penetration of antibiotics into closed foci in gonorrhoea, 64 male patients with acute gonorrhoea were divided into 2 series; one received tetracycline phosphate equivalent to 750 mgm. of hydrochloride orally in a single dose and the other the same together with 12 mgm. methyl prednisolone. The immediate failure rate with the former was 14.3% and with the latter 13.3%. No side effects or complications were seen.

Follow-up was mostly for relatively short periods and there were numerous reinfections (or relapses).

It is concluded that methyl prednisolone does not assist tetracycline in the treatment of gonorrhoea.

T. E. Osmond

CSONKA, G. W. & FURNESS, G. **A Study of the Aetiology of Non-Gonococcal Urethritis and Reiter's Disease.** *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 181-5. [16 refs.]

This article contains so much technical detail which cannot be included in an abstract that it should be studied in the original. Briefly, 17 male patients suffering from non-gonococcal urethritis (NGU) and 3 suffering from Reiter's disease were investigated; most had had previous attacks of NGU or gonorrhoea or both, they were nearly all aged 20-30 years, incubation periods varied from 5 days to 3 months (usually about 12 days) and response on the whole was poor to streptomycin and sulphadiazine but good to achromycin.

PPLO (pleuro-pneumonia-like organism) media and chick embryo cell cultures were inoculated and the latter were stained with Macchiavello's stain. No evidence was found of deterioration in cell cultures of specimens from NGU patients, nor were inclusion bodies seen; PPLO were grown from 2 cases of NGU.

One typical case of Reiter's disease was fully investigated; this patient had urethritis, conjunctivitis, balanitis and arthritis; urethral cultures showed an abundant growth of PPLO and cytopathic deterioration occurred sporadically in some of the chick embryo cell cultures; cultures from conjunctiva and mouth were negative and a virus aetiology was therefore not considered likely; CF tests of serum against PPLO showed a rising titre as the disease progressed. It is concluded that PPLO could be ignored, as could a virus, as the cause of NGU unless failure to demonstrate the latter was due to sub-optimal conditions. [The results of this investigation are essentially negative but the article is well worth study.]

T. E. Osmond

RODIN, P., KING, A. J., NICOL, C. S. & BARROW, J. Flagyl in the Treatment of Trichomoniasis. *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 147-51.

These authors treated 82 women and 38 men suffering from trichomoniasis with Flagyl (8823 RP) (1- β -hydroxyethyl-2 methyl-5 nitro-imidazole), 200 mgm. by mouth 3 times a day for 7 days; 11 of the women also had gonorrhoea. Of the 82 women 78 (95%) showed immediate response and of 52 followed for 3 months 43 (83%) showed success. Symptoms and signs improved rapidly, the vaginal pH fell from 5.5-6.4 to 4.9-4.6 in 1 to 2 weeks, pus cells decreased and no effect on *Candida* was apparent. Estimations of Flagyl concentrations in urine, serum and saliva were made in a few cases and it was noted that these were lowest in patients who did not react to treatment.

Of 38 male partners 11 showed trichomoniasis, 14 had non-specific urethritis and 4 had gonorrhoea; 20 males infected with trichomonas vaginalis were treated in the same way as the women and all were apparently cured; observation extended over 2-16 weeks; 4 men who showed only partial response were found to be suffering from stricture (2) litritis and prostatitis. Side effects were negligible except in 1 case where a rash appeared on arms, chest and back and lasted 6 days.

White blood counts were done in 41 cases and in 3 the polymorphonuclear leucocytes fell slightly below the normal lower limit but only temporarily. Failure of treatment appears to be related to low serum concentration of the drug either through failure to take the drug, deficient absorption or over-rapid excretion.

T. E. Osmond

NICOL, C. S., BARROW, J. & REDMOND, A. Flagyl (8823 RP) in the Treatment of Trichomoniasis. *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 152-3.

Flagyl [see above] was employed in the treatment of 127 female and 11 male patients suffering from trichomon-

iasis; dosage was 200 mgm. 3 times a day for 5 days; of the 127 females 122 completed treatment; 105 showed apparent cure and 17 failed; of these 17 failures, 5 were detected in less than 1 month, 7 in 1 to 3 months and 5 in more than 3 months; 12 admitted sexual intercourse; 1 patient vomited and had to stop treatment. Of the 11 males all were apparently cured.

Assays of Flagyl in the 24-hour urine during the 5 days of treatment carried out on 1 patient showed 160-480 μ gm./ml. (polarographic), excretion 170-370 mgm. (calculated from the polarographic figures) and 160-320 μ gm./ml. (bio-assay); in serum the figures were 3.2-3.9, 10 and 7.6 μ gm./ml. on the first, third and fifth days (polarographic assay) and 10 μ gm./ml. (bio-assay) on the first day.

T. E. Osmond

DUREL, P., COUTURE, J., COLLART, P. & GIROT, C. Flagyl (Metronidazole). *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 154-7, 2 figs. Discussion 157-62.

These authors favour simultaneous local and systemic use of this drug. For the former they recommend a 500 mgm. pessary every evening for at least 10 and preferably 15-20 days together with a bland vaginal douche every few days. Their failure rate with pessaries alone was 32.5% but if patients re-treated successfully are included the rate is 7.9%. For oral administration the dosage was 250 mgm. twice a day for 10 days and with this the failure rate was 26%. There were no toxic effects with local and only a few mild ones with oral treatment. As regards urinary excretion after oral treatment, experiments showed that after a single oral dose of 1 gm. excretion is rapid and continuous, starting after about 5 hours and being nearly complete after about 72 hours. Further experiments showed that Flagyl has no effect on the fertility of rats and does not alter the blood picture in human beings.

In the discussion which followed most agreed closely with the results reported in the foregoing 3 papers, success rates with oral Flagyl being 86-96%; side reactions tended to increase with dosage: several reported the presence of *candida* species after treatment but these do not seem to have had any appreciable harmful effects.

Two of the difficult problems encountered were the differential diagnosis of relapse and reinfection and the tracing, diagnosis and treatment of (male) contacts.

T. E. Osmond

WATT, L. & JENNISON, R. F. Incidence of *Trichomonas vaginalis* in Marital Partners. *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 163-6. [13 refs.]

These authors examined 30 husbands of women suffering from trichomonal infection and 50 random male patients attending a venereal diseases clinic. Of the study group of 30, 18 (60%) showed *trichomonas vaginalis* in cultures; the prostatic fluid gave most positive results, followed closely by urine and urethral discharge; with the preputial sac a bad fourth; 11 (61%) of the positive males showed no clinical abnormality. Of the control

group of 50, 14 had no abnormality, 21 had non-gonococcal urethritis, 14 had gonorrhoea and 1 had cystitis; 4 (8%) showed *trichomonas vaginalis* in cultures of the prostatic fluid (3 of these 4 were coloured men).

From the foregoing it seems clear that trichomoniasis is frequently transmitted during sexual intercourse but there is a good deal of evidence that this is not the only way.

It is of interest to note that a study of the literature discloses that 5.8% to 68% of males harbour the organism though this last figure is highly suspect. Cultures are undoubtedly the most effective methods of revealing the organism and in males the prostate seems to be the commonest source.

T. E. Osmond

WILLCOX, R. R. Epidemiological Aspects of Human Trichomoniasis. *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 167-74, 3 figs. [36 refs.]

This is a most informative article which goes well beyond its title. Trichomonads, human and otherwise, are widespread in nature, occurring in termites, fish, reptiles, birds (26 kinds) and mammals (24 kinds). Those which occur in man are *T. vaginalis*, *T. buccalis* and *T. hominis*; only the first named is of clinical importance, though the possible transmission of trichomonads from animals or birds to man with a resulting modification in appearance, cannot be ruled out.

The incidence of *T. vaginalis* in women has been variously estimated: it tends to be higher in pregnant than non-pregnant women, in negroes than in whites, in the middle 15-60 age-groups than in the young and old and in those with venereal diseases and gynaecological conditions than in the general population; probably the figure for sexually-active females lies between 10 and 25%. Males are affected apparently much more rarely, probably only 1 for every 1,000 females. The condition is usually spread by sexual intercourse, but indirect means include lavatory seats and towels, baths, swimming baths, flies, etc., but these are unlikely sources of infection.

Conditioning factors include local trauma and infection with other organisms; poor personal hygiene and generally low social-economic conditions favour spread of infection and psychological factors should be taken into account: it is of interest to note that Roman Catholics are apparently less often affected than Protestants.

Why trichomoniasis is so much more common in women than in men is unknown.

T. E. Osmond

WILLCOX, R. R. An Imidazole Derivative (Flagyl) Effective Orally in Vaginal Trichomoniasis. *Brit. J. Venereal Dis.* 1960, Sept., v. 36, No. 3, 175-7.

This author treated 40 female patients suffering from vaginal trichomoniasis with Flagyl [see above]; the dosage was 200 mgm. orally 3 times a day for 7 days (8 took it for only 5 or 6 days); 14 had had previous attacks of trichomoniasis, 8 of gonorrhoea and 2 of syphilis; 10 were found to have gonorrhoea and were treated with penicillin. Of 34 patients followed only 2 showed immediate failure; both these failed to react to additional

treatment. In addition there were 6 recurrences; of 101 post-treatment observations made from 3 to more than 90 days after treatment, positive findings were recorded in only 10. 2 patients required local treatment for vaginal thrush after 15 and 60 days and 3 had vaginitis (without trichomonads) after 54, 56 and 70 days respectively. There were no side effects of treatment. The male consort of 3 of the failed patients were examined but showed no trichomonads. The failure rate of 5.9% is contrasted with that of 90.2% with trichomycin and 100% for aminotrozole.

T. E. Osmond

(i) **WATT, L. & JENNISON, R. F. Clinical Evaluation of Metronidazole. A New Systemic Trichomonicide.** *Brit. Med. J.* 1960, Sept. 24, 902-5. [13 refs.]

(ii) **REES, Elisabeth. Systemic Treatment of Trichomonas vaginalis Infestation in Women. A Preliminary Report.** *Brit. Med. J.* 1960, Sept. 24, 906-9.

(iii) **MOFFETT, Mary & MCGILL, M. Isabel. Treatment of Trichomoniasis with Metronidazole.** *Brit. Med. J.* 1960, Sept. 24, 910-11.

These 3 papers may be considered together since they all deal with the same subject, *i.e.* the systemic treatment of trichomoniasis with metronidazole (1- β -hydroxyethyl-2 methyl-5-nitromidazols) known as "flagyl" [*this Bulletin*, 1959, v. 34, 626; 1960, v. 35, 992; 1961, v. 36, 145, above].

(i) Watt and Jennison treated 50 patients with 200 mgm. 3 times a day for 1 week; 44 were apparently cured (88%) and 6 failed; of these latter 3 were cured by a higher dosage, 1 could not tolerate this and 2 defaulted. Side effects occurred in 11 patients on the lower dosage and in all on the higher dosage; they were mostly mild and affected the gastro-intestinal tract. An interesting point is that it was shown that 9 out of 14 strains of trichomonads were sensitive *in vivo* to a strength of 1 in 4 million of the drug.

(ii) Rees treated 19 patients with 200 mgm. 3 times a day for 7 days; of 14 acute cases 11 were apparently cured, 2 showed no response but reacted to a second course of treatment and 1 was "not recorded". Of 19 subacute cases 8 were apparently cured, 7 were much improved, 2 showed no response and 2 were "not recorded".

Of 6 "carrier" cases, 2 were positive after 1 week but the other 4 were negative after 2 weeks; however 2 were positive after 6 weeks and may have been reinfected. Toxic reactions occurred in 5 patients 1 of whom developed a rash. 10 male patients were also treated. 15 of 39 cases also had gonorrhoea; this possibility must be borne in mind otherwise the diagnosis may be missed when symptoms disappear under the effect of "flagyl" therapy.

(iii) Moffet and McGill treated 42 patients with 200 mgm. 3 times a day; the first 14 received the drug for 10 days with a 0.5 gm. pessary each night: the next 24 had oral treatment only and the last 4 were treated for only 7 days: 26 of the patients had gonorrhoea as well.

40 of the patients were cured and 2 failed; it is assumed that in these 2 longer treatment was necessary.

Flagyl had no effect on *Candida albicans*, in fact this may be encouraged by the elimination of trichomonads.

It is important that the husbands or other sexual partners of patients should be treated concurrently, otherwise reinfection may occur and simulate relapse.

There is little doubt that this drug is effective but longer experience is necessary before its effects can be fully evaluated. It is of interest to note that where cultures as well as films were employed in tests of cure the former were more often positive than the latter

T. E. Osmond

GENERAL INFECTIVE DISEASES

The order in this section is:—General; Hospital and other Cross Infections; Coccid Infections; Bacterial Infections; Virus Infections.

GENERAL

CASON, J. S. & LOWBURY, E. J. L. Prophylactic Chemotherapy for Burns. Studies on the Local and Systemic Use of Combined Therapy. *Lancet*. 1960, Sept. 3, 501-7. [14 refs.]

This paper from the Birmingham Accident Hospital describes studies of 3 methods of treating burns with anti-bacterial agents. In the first the effect of applying a cream containing neomycin, chlorhexidine and polymyxin (NCP) to burns of not more than 15% of the body surface was compared with that of applying simple tulle gras in one series and penicillin cream in another. NCP cream was decidedly superior to tulle gras as judged by the frequency of colonization of the burns by each of 5 varieties of bacteria (the largest differences being for *Streptococcus pyogenes* and *Staphylococcus aureus*), by the frequency of successful takes of grafts, and by time in healing. The numbers of patients in the series in which NCP and penicillin creams were compared were smaller, and the results are not analysed in the same detail, but the results with NCP cream were better in regard to graft takes and in that fewer patients so treated developed infections requiring systemic chemotherapy.

The second study was in patients with more extensive burns liable to be complicated by septicaemia, and consisted of comparing the effects of systemic treatment with penicillin on the one hand and the combination of chloramphenicol, tetracycline, erythromycin and polymyxin on the other. No patient became infected with *Str. pyogenes*: infections with staphylococci, *Pseudomonas* or *Proteus* were commoner in the combined group and infection by coliforms in the penicillin group. In the penicillin group (12 patients) and the combined group (11), the numbers of deaths were 9 and 6 respectively, of clinical septicaemia 6 and 3, and of respiratory complications 7 and 3. Some discouraging particulars are given of the frequency of resistance to antibiotics in staphylococci from these patients: in the combined group the percentage of the strains resistant to chloramphenicol reached 71% at one stage, and 100% at some stage to tetracycline and erythromycin. In the penicillin group resistance particularly to chloramphenicol and except to penicillin, was less frequent.

The third study concerned only burns infected with *Str. pyogenes*, and it is recorded that although treatment

of this infection with either tetracycline or erythromycin has in the past been followed by the appearance of antibiotic resistance, no resistance to either has been seen in the 2 years since treatment with both of these antibiotics together in full doses was started.

L. P. Garrod

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 198. European Technical Conference on Control of Infectious Diseases through Vaccination Programmes, Rabat, Morocco, 23-31 October 1959. Report. 21 pp. 1960. Geneva: Palais des Nations. [Sales agent for U.K. H.M. Stationery Office.] [1s. 9d.; \$-30; Sw.fr. 1.-.]

This conference was attended by 24 member representatives of the European countries, together with the WHO secretariat and Morocco observers, with Professor Zhdanov, Vice-Minister of Health of the U.S.S.R., as chairman. The present practices relating to the control of infectious diseases through vaccination programmes in the various European countries were first considered and these are briefly summarized in the report. In dealing with organization, the conference discussed the arrangements for implementing vaccination programmes, individual card records of immunization, costs and the role of health education. In dealing with immunization against the various infectious diseases, smallpox, tuberculosis, poliomyelitis, diphtheria, tetanus and pertussis were first discussed. Full consideration was given to the two main types of poliomyelitis vaccines—the inactivated and the attenuated live virus vaccines. It was unanimously agreed that the use of the triple diphtheria-tetanus-pertussis vaccine should be promoted but the inclusion of polio antigens to form a quadruple vaccine was not recommended.

Immunizations used occasionally or in selected population groups comprised vaccines against enteric fevers, leptospirosis, tick-borne encephalitis, tularaemia, brucellosis and rabies together with influenza, mumps and measles. Yellow fever, typhus and cholera were considered separately as quarantinable diseases.

In dealing with vaccination against enteric fevers it was stressed that control of these diseases by such means should be considered only as an activity supplementary to sanitation programmes and the raising of the general standard of hygiene. Based on the results of the recent

Yugoslav field trials the phenolized TAB vaccine was recommended until more reliable information was available about other preparations or a better vaccine has been devised. The need for further research in this field was emphasized.

In discussing the risks of immunization procedures first place was given to the sterilization of the syringe and needle. This followed the accustomed lines—dry heat sterilization, sterile syringe service etc.—but it was clear that the more usual method employed was the boiling of both the syringe and needle for 10 minutes immediately before use. The cheap disposable syringe had a brief mention. Of the other risks, the influence of alum-containing prophylactics in provoking paralytic poliomyelitis was considered and also the complications of smallpox vaccination.

The actual schedule of immunizations suggested was very similar to those agreed to at recent conferences on the same subject held in London and Paris [this *Bulletin*, 1960, v. 35, 1110, 1111] particularly with regard to immunization against diphtheria, tetanus, pertussis and poliomyelitis. Smallpox vaccination was recommended at 6–7 months at this conference whereas the British conference considered, in the absence of special risks, that any time during the first five years of life would be satisfactory.

The report is very brief and appears to be an able summary of the business conducted. *H. J. Bensted*

GALLOWAY, T. McL. A Record and "Claim" Card for Vaccination and Immunization Procedures. *Med. Officer*. 1960, Oct. 28, v. 104, No. 18, 263–4.

HOSPITAL AND OTHER CROSS INFECTIONS

PUBLIC HEALTH LAB. SERVICE. Incidence of Surgical Wound Infection in England and Wales. A Report. *Lancet*. 1960, Sept. 24, 659–63.

In order to obtain a representative estimate of the incidence of post-operative wound infection, a survey was made of the course of a total of 3,276 surgical patients in 22 hospitals. Clinical and bacteriological observations were made during convalescence and the final assessment was the joint responsibility of the surgeon and bacteriologist. All the patients admitted to the surgical wards concerned during the study period were included except those with frank sepsis (other than peritonitis) or with operations of the rectum, urinary or genital tract.

Of 2,746 wounds (excluding those in patients with peritonitis) with complete clinical and bacteriological records, 14% showed some signs of clinical sepsis during healing, and a total of 24% yielded pathogenic bacteria on culture; 11% were septic and yielded pathogens on culture. Almost half the wounds classed as septic discharged frank pus. *Staph. aureus* was found in 60% of the septic wounds; coliform organisms were found in a total of 30%. 19% of the "septic" wounds, but only 6% of the purulent wounds, yielded no pathogens on culture.

The incidence of sepsis with infection varied from 22% to 5% in the general hospitals; 1 orthopaedic hospital had a rate of 1%. Gall bladder and breast operations had the highest sepsis rates, apart from operations in patients with peritonitis; thyroid and orthopaedic operations had among the lowest rates. There was no difference in the overall sepsis rates in males and females, but increasing age, duration of operation and length of incision, as well as the presence of drainage, were all associated with increased sepsis rates. The sepsis rate was not significantly greater in nasal carriers of *Staph. aureus* than in non-carriers, although nasal carriers of a few particular types had an above-average experience of infection. The sepsis rate increased with prolongation in the patients' pre-operative stay in hospital.

At the end of each operation the surgeon made an estimate of the patient's expected stay in hospital. For patients with uninfected and healthy wounds the surgeon's predictions were very accurate: the observed stay was on average 0.8 days less than the predicted. Patients with septic and infected wounds had an average actual stay 7.3 days in excess of expectation. For the whole group of patients the excess stay in hospital was 1,772 days, or 5.8%, the probable uncomplicated stay. Only 1 patient died as a result of sepsis.

It is calculated that, if the figures obtained from this survey are applicable to the 1.5 million surgical operations performed in hospitals in England and Wales, the total excess stay may be about 1 million bed days per year. This is about 3% of the total bed occupancy of acute hospitals and might represent a cost of some £3.3 million. *R. E. O. Williams*

SUSSMAN, M. & STEVENS, J. *Pseudomonas pyocyanea* Wound Infection. An Outbreak in an Orthopaedic Unit. *Lancet*. 1960, Oct. 1, 734–6, 2 figs.

An epidemic of post-operative wound infection due to *Pseudomonas pyocyanea*, involving 8 patients in an orthopaedic unit, was traced to the use of unsterilized cellulose wadding for padding plaster casts applied to compound fractures or simple fractures in patients with skin abrasions. This was heavily contaminated. An Esmarch bandage used in the operating theatre was heavily contaminated with other organisms, but not with *Ps. pyocyanea*, but the bucket used for soaking plaster bandages was found to be contaminated with *Ps. pyocyanea*. The infection commonly led to full-thickness skin loss. The wadding could be sterilized by autoclaving without causing serious deterioration. *R. E. O. Williams*

SHOOTER, R. A., GIRLING, J. A., MATTHIAS, J. Q. & WILLIAMS, R. E. O. Staphylococcal Infection in a Medical Ward. *Brit. Med. J.* 1960, June 25, 1923–4.

A pilot survey was made of staphylococcal sepsis in a 26-bed medical ward during the year, October, 1958 to September, 1959.

Of 349 patients, 9 (2.6%) were admitted with staphylococcal sepsis and 13 (3.8%) of the remainder developed it. Of these 22, 9 had lower respiratory infection, one

case progressing to empyema and another to lung abscess, 9 had infection of skin and subcutaneous tissues, 2 had enterocolitis, 2 had terminal septicaemia and there was 1 case each of sinusitis, urinary infection, and mouth ulceration (3 patients had 2 incidents each). In 90 patients with malignant or blood disease 13 (14%) developed sepsis compared with only 9 (3%) of the 259 patients who had neither.

There was no evidence of infection spreading from patient to patient since only 2 were infected with any one staphylococcal phage type. Of those developing sepsis in hospital, 7 patients yielded the same type of staphylococcus as had been present in admission nasal swabs and 6 yielded types not isolated at any time from the nose. In no case did a patient develop sepsis from a nasal strain of staphylococcus acquired in hospital [see also WILLIAMS *et al.*, this *Bulletin*, 1960, v. 35, 467].

In view of the low cross-infection rate in the ward under survey, a spot check was made of 243 patients in medical wards of the hospital. Of these only 8 had staphylococcal sepsis and there was no evidence of a common type in any ward.

J. G. Hutchison

MACFARLANE, D. A., MURRELL, J. S., SHOOTER, R. A. & CURWEN, M. P. **Staphylococcal Sepsis in Out-Patients. Relation of Penicillin Resistance to Previous Contact with Hospitals.** *Brit. Med. J.* 1960, Sept. 24, 900-902.

Swabs taken from septic lesions in 208 patients attending the casualty department of a London hospital yielded *Staph. aureus* in 170 cases, 39% of the staphylococci were penicillin-resistant. This is compared with a rate of 6% reported from the same hospital in 1949-50 [this *Bulletin*, 1950, v. 25, 298], and one of 25% reported in 1957 [*ibid.*, 1958, v. 33, 61]. 5 strains were resistant to tetracycline. The proportion of lesion staphylococci resistant to penicillin was 69% in 13 patients who had been hospital in-patients, and 49% in 65 who had been out-patients, within 12 months; 62% in 13 from families with babies born in hospital within 12 months; and 58% in the 24 with a family contact who had been in hospital. It was 65% in 20 who had had antibiotic treatment within 3 months. 76 patients in none of the above categories gave a frequency of penicillin-resistant strains of only 24%.

65 of the 170 patients reported a previous similar septic lesion within 12 months. The nasal carriage rate for *Staph. aureus* for the septic patients was 71% and for 214 control patients, 34%; 42% and 32% respectively of the staphylococci were penicillin-resistant.

R. E. O. Williams

MAYER, G. & SOMPOLINSKY, D. [Infections due to *Staphylococcus aureus* in a Maternity Unit] *Harefuah*. Jerusalem. 1960, Oct. 16, v. 59, No. 8 [in Hebrew 240-42. (19 refs.) English summary 244].

The English summary appended to the paper is as follows:—

"The results of examinations for *Staphylococcus aureus* in newborns, their mothers, the medical staff and

the surroundings in a big maternity unit troubled with staphylococcal infections in newborns, are analyzed.

"In 92% of the newborns, *S. aureus* was isolated from the umbilicus, feces, and/or nose. 38 epidemiological types were recognised, but only 4 of them were very frequent (83% of all strains). In most of the cases, more than 1 staphylococcal type was isolated from the newborn, from a single or from different sites.

"The carrier rate of the mothers (nose and vagina) before delivery was very low (3.7%). The types of staphylococci found in the newborns showed no correspondence with those found in the midwives.

"The authors conclude that the source of the infection is to be found inside the infants' room, with spread from infant to infant, and from the staff of these rooms to infants. Bad hygienic conditions, especially overcrowding, may have been an essential factor in spreading the infections."

FARRER, S. M. & MACLEOD, C. M. **Staphylococcal Infections in a General Hospital.** *Amer. J. Hyg.* 1960, July, v. 72, No. 1, 38-58, 4 figs. [20 refs.]

The staphylococcal infections which occurred, in the absence of an epidemic, in a large general hospital in Philadelphia between March 1958 and February 1959 are analysed. Clinically infected people were divided into 3 groups:—

- (a) those who acquired the disease in that hospital (319);
- (b) those admitted with staphylococcal disease (287), 45.9% of whom gave a history of recent hospitalization;
- (c) hospital personnel.

The authors point out that they have not included infections which developed after discharge from hospital.

The greatest number of patients in group (a) were in the 6th decade of life; the attack rate was higher in males than females, and in public ward patients than others. White patients accounted for nearly twice as many infections as non-whites, 80% of these patients had some chronic disease (diabetes mellitus, fractures, malignant disease) and the mean time of onset was 18.6 days after admission. 60.8% of infections in this group were wound infections, 65% of them associated with clean procedures; the mean time between operation and development of sepsis was 9.8 days, suggesting that infection was acquired in the ward rather than at operation. 57.6% of these patients had a prolonged stay in hospital as a result of infection.

Of the patients in group (b), 45.3% had skin lesions and 16.4% respiratory tract infections. All patients in group (c) had skin infections and the infection rate was highest among student nurses (28.8%).

There were 9.9% deaths associated with staphylococcal disease in the hospital during the period of study, the majority of which were from respiratory tract infections. 82% of strains from group (a) patients were bacteriophage-typed, about one-third of these and one-third of the strains from group (b) patients were type 52/42B/80/81 [strains probably identical with type 80/81 in Britain].

M. Patricia Jevons

WOLINSKY, E., LIPSITZ, P. H., MORTIMER, E. A., Jr. & RAMMELKAMP, C. H., Jr. **Acquisition of Staphylococci by Newborns. Direct versus Indirect Transmission.** *Lancet*. 1960, Sept. 17, 620-22, 1 fig.

A study was made in a 7-cot nursery in a maternity hospital in Cleveland, Ohio. An "index" infant known to be carrying a typable strain of *Staphylococcus aureus* was placed in one cot and the others were filled with normal newborn infants who remained in the room for 48 hours. The index infant was tended by nurses from outside the study nursery; the others were tended by 1 of 3 nurses (2 of whom carried staphylococci) on duty in the room. A different index baby was employed each week. In all 91 infants were exposed; 1 became infected with a strain identical with that carried by the index infant and 7 with strains probably the same.

On the other hand 21 of 95 infants acquired the strain carried by nurse A (type 52/52A/80/81) and 12 acquired the strain carried by nurse B (type 3A/3B/3C).

During 2 weeks when nurse A took no active part in tending the infants, but sat in a chair in the nursery, no infants acquired her staphylococcus. Conveyance of the nurses' staphylococci by handling was also demonstrated when nurses tended infants in incubators supplied with fresh air from outside the nursery. It is concluded that personnel-to-infant spread of staphylococci is the predominant route, and that infant-to-infant spread is of lesser importance.

[It would be valuable to have analogous studies carried out in other hospitals for there are several records of extensive spread of particular types of staphylococci in nurseries in which no carrier among the personnel could be discovered.]

R. E. O. Williams

EICHENWALD, H. F., KOTSEVALOV, Olga & FASSO, Lois A. **The "Cloud Baby": an Example of Bacterial-Viral Interaction.** *Amer. J. Dis. Children*. 1960, Aug., v. 100, No. 2, 161-73, 11 figs. [14 refs.]

265 newborn infants in a New York hospital carrying *Staph. aureus* in the nose, 49 of whom also had staphylococcal skin lesions, were examined for dispersal of staphylococci into the air. The infants, dressed only in a paper diaper, were placed in an unventilated airtight cubicle of 150 cu. ft. volume. Air was collected with impinger samples placed 12 inches from the infant after it had remained undisturbed for 1 hour. 38 of the 49 babies with skin lesions yielded air counts of 6 or more staphylococci per 10 cu. ft. 112 of 216 normal infants yielded counts of this magnitude; such asymptomatic infants are referred to as "cloud babies".

Most of the staphylococci appeared to be liberated in particles 5μ in diameter or less. When the infants' bodies were enclosed in polythene bags, tied loosely round the neck, there was no reduction in dispersal by the cloud babies; many of the babies with skin lesions, however, yielded a lower count under these circumstances.

There was some indication that the presence of cloud babies might be associated with epidemic spread, and on two occasions the development of "cloudiness" in

a baby, or the inadvertent introduction of a cloud baby into an unaffected nursery, was followed by epidemic spread. The development of cloudiness among the babies was rapidly followed by an increase in the air count of staphylococci, and by spread of the epidemic type to the nursery.

It was then observed that the transfer of infants who were not carriers of staphylococci from a nursery suffering a cloud-baby outbreak to an unaffected nursery was followed by the development of the cloudiness by 2 erstwhile non-disseminating carriers. In seeking a cause for this it was found that in all of 5 cloud babies from one outbreak, there was evidence of adenovirus type 2 infection; and in all of 5 from a second outbreak, ECHO type 20 virus was isolated. None of 5 babies from a 3rd outbreak yielded a virus.

There was no excess staphylococcal disease in cloud babies as compared with non-disseminating carriers, but among the household contacts of cloud babies the incidence of sepsis was 24% as compared with 6% for the contacts of the non-disseminators.

It is concluded that the peculiar ability to spread staphylococci characterizing a proportion of the infants, and perhaps attributable to concomitant virus infection, is an important cause [but not, the authors stress, the only cause] of nursery outbreaks of staphylococcal infection. The possible role of air disinfection and efficient ventilation in prevention is emphasized.

[This is an important contribution and may well offer a satisfying explanation for some of the differences in the behaviour of staphylococci introduced into maternity nurseries.]

R. E. O. Williams

ELEK, S. D. & FLEMING, P. C. **A New Technique for the Control of Hospital Cross-Infection: Experience with BRL 1241 in a Maternity Unit.** *Lancet*. 1960, Sept. 10, 569-72, 4 figs.

Nasal swabs taken from 58 babies in 2 maternity wards showed 48 (83%) of them to become nasal carriers of *Staphylococcus aureus* in the first 10 days of life, most becoming carriers within 5 days of birth. In an attempt to control the nasal acquisition of staphylococci a solution of 1 gm. Celbenin (BRL 1241) [see below, pp. 173-5] in 20 ml. water was sprayed into the air of the nursery once daily. Of 29 babies nursed in the unit under this regime, only 12 (41%) became carriers. Subsequently 58 babies were observed during a period when the antibiotic was sprayed into the air 4 times a day. Only 14 (24%) were ever shown to be carriers (in daily swabbings) and most of these carried *Staph. aureus* only transiently. Although no systematic observations were made, there seemed also to be some reduction in the frequency of skin carriage.

In 6 months during which Celbenin was sprayed into the air 4 times a day approximately 170 babies were observed in the test and in a control nursery; there were 14 minor septic lesions in babies in the control nursery but none in the test nursery. The dust in the ward at the end of 6 months was found to have an inhibitory concentration corresponding to 200 μ gm. Celbenin per gm., but no *Staph. aureus*. No resistant strains of *Staph. aureus* were encountered.

[The scientific interest of the observations is undoubted; the extent to which the method can be applied in routine practice must clearly depend on the importance with which the rare Celbenin-resistant strains are regarded.]

R. E. O. Williams

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus*, *Streptococcus*, *Neisseria*, *Others*.

COPPO, A., PETRONE, M. & UNGARI, S. Studio dei portatori di *M. pyogenes* tra i pazienti di una clinica pediatrica. [*Staphylococcus pyogenes* Carriers among the Patients of a Pediatric Clinic] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Mar.-Apr., v. 11, No. 2, 77-89. English Summary.

In 9 tables the authors give the results of an investigation carried out by nasal and anal swabbing on 97 children up to 12 years of age who were patients at the pediatric clinic of the Umberto I Polyclinic in Rome. 14 patients were swabbed twice. Staphylococcal strains which produced yellow colonies on Chapman's medium, which were haemolytic on rabbit blood agar and had a typical microscopical appearance, were considered positive. The reports include phage type, coagulase, gelatin and mannite tests and antibiotic sensitivity.

The findings confirm the view that children carry staphylococci more frequently than adults [this *Bulletin*, 1960, v. 35, 153], 77.3% of those examined being positive, 97% of children under 3 being nasal carriers and 72% being anal carriers. Unlike the findings with adults there was notable agreement between the types isolated from both sources. Most of the strains belonged to phage types in group III, being mainly type 47. Others were susceptible to phages 29, 52 and 52a, belonging in group I, these latter being as a rule more sensitive to antibiotics. Only 1 strain was resistant to novobiocin and that only partially.

E. Agius

HAY, D. R. *Staphylococcal Septicaemia and Pyaemia.* *Quart. J. Med.* (n.s.) 1960, July, v. 29, No. 115, 313-31, 3 figs. on pl. [18 refs.]

During 1957 and 1958 a total of 59 patients were found to yield *Staph. aureus* from blood cultures in a hospital in Christchurch, New Zealand; this represented a substantial increase over the number recognized in previous years. 14 additional cases of staphylococcal pyaemia were recognized at post-mortem. Of 71 patients studied [the discrepancy in the figures is not discussed], 36 died. 25 patients were aged 61 or over and 18 of these died.

In 20 patients the septicaemia followed a surgical operation and a focus of infection either in wound or intravenous-drip site was always demonstrable; 15 of the patients died. The patients had often been in hospital for a long time and several had had more than one post-operative complication. 16 patients had osteomyelitis

and 2 of them died. 10 patients, of whom 4 died, had septicaemia following an infection of the head or neck; in several cases the primary focus was not easily identified. 4 infants had septicaemia following umbilical sepsis and all died. 6 patients had staphylococcal endocarditis and all died.

Altogether 10 of the 71 patients suffered from diabetes; their septicaemia usually arose from a fairly obvious cause. 12 of the patients showed some cerebral involvement during life; 8 of them died. 31 showed pulmonary consolidation and 18 of these died.

20 of the 71 patients were infected with penicillin-sensitive staphylococci; the proportion was 9 out of 16 in the patients with osteomyelitis. 27 of the patients are thought to have acquired their infection in hospital.

There is extended discussion of the treatment, with emphasis on the need for early diagnosis.

R. E. O. Williams

HINTON, N. A., TAGGART, J. G. & ORR, J. H. *Diagnosis of Staphylococcal Enteritis.* *Canadian Med. Ass. J.* 1960, Sept. 24, v. 83, No. 13, 700-704. [14 refs.]

The authors found in a survey in Kingston, Ontario, that 17% of adult patients without intestinal disease were intestinal carriers of coagulase-positive staphylococci: in a group of patients in hospital for a long time who were given antibiotics the rate rose to 40%. In children they found carrier rates of between 40 and 80% [this *Bulletin*, 1961, v. 36, 50]. Obviously the demonstration of staphylococci in the faeces is insufficient for the diagnosis of staphylococcal enteritis.

Studying 19 cases of enteritis associated with staphylococci in the faeces, the authors found several epidemiological and clinical patterns. Some patients developed severe diarrhoea in hospital after the use of antibiotics: of these, some died, others recovered after being given another antibiotic. Some patients similar to the above but with less severe symptoms recovered when the antibiotic was stopped. Other patients both inside and outside hospital developed diarrhoea without the use of antibiotics: some recovered after being treated with antibiotics, others without antibiotics. Not all diarrhoeas occurring after antibiotics are staphylococcal and not all staphylococcal diarrhoeas are post-antibiotic. Even a pure culture of staphylococci may be found in the faeces in the absence of diarrhoea, but the absence of staphylococci from the faeces does rule out staphylococcal diarrhoea. All these points must be considered in the diagnosis. It is not doubted that many severe diarrhoeas occurring after antibiotics are caused by staphylococci nor that administration of antibiotic and the presence of staphylococci in the faeces are closely related but there are several factors in the pathogenesis not yet understood.

A. B. Christie

MCCOY, K. L. & KENNEDY, E. R. *Autogenous Vaccine Therapy in Staphylococci Infections.* *J. Amer. Med. Ass.* 1960, Sept. 3, v. 174, No. 1, 35-8.

In 60 cases of staphylococcal infection, treatment with autogenous vaccine produced excellent response in 44,

improvement in 11, and failure in 5. 50 of the patients had furunculosis and were treated as out-patients: the other 10 were in-patients and had various septic conditions. Details are given of only 4 patients. 10 injections formed a course and were given intracutaneously. The authors stress the importance of the method of preparation of the vaccine:—a mild killing agent should be used instead of heat, vaccine should be made from original exudate without subculture, vaccine density should be standardized before killing and vaccine should be shaken periodically during incubation to promote autolysis and liberation of cellular elements. *A. B. Christie*

BREESE, B. B., DISNEY, F. A. & TALPEY, W. B. **The Prevention of Type Specific Immunity to Streptococcal Infections due to the Therapeutic Use of Penicillin. Occurrence of Second Attacks due to the Same Type of Group A Hemolytic Streptococci.** *Amer. J. Dis. Children.* 1960, Sept., v. 100, No. 3, 353–9. [20 refs.]

An intriguing question is now being clarified—does the extensive use of penicillin in the treatment and prophylaxis of Group A streptococcal infections lead to loss of immunity and consequent increase of the disease in older persons?

3,047 children were observed for streptococcal attacks over the 10-year period 1947–57. A total of 6,198 attacks occurred, about 51% of the children having only a single attack, 23% two attacks, 11% three attacks, and the remainder more than three. Type 12 was responsible for 46% of the recurrences, type 1 for 13%, and types 6 and 28 for 10% each. It is thus evident that there is considerable individual loss of type specific immunity. On the other hand the percentage rate of attack in relation to age-groups remained relatively stable during the period. In this population, therefore, although there were recurrences in individual cases, there was no loss of the expected immunity with increasing age. It would seem that fears that the extensive use of penicillin would ultimately lead to a non-immune adult population are unfounded.

H. Stanley Banks

DAVIES, A. M. & LAZAROV, E. **Heredity, Infection and Chemoprophylaxis in Rheumatic Carditis: an Epidemiological Study of a Communal Settlement.** *J. Hygiene.* 1960, Sept., v. 58, No. 3, 263–76, 2 figs. [25 refs.]

A kibbutz is a farm settlement in Israel in which there is a strict social framework which includes the communal rearing of children. Environmental factors are common to all the members so that, in the study of the incidence of streptococcal infections and rheumatic episodes within the group, environmental factors can be excluded. The authors studied the members of a kibbutz, including 104 children aged 18 months to 10 years, for 14 months. Children with proven heart disease showed, in spite of continued penicillin prophylaxis, the same streptococcal carrier rate as controls and the prevalence of rheumatic heart disease in children with rheumatic parents was 2½ times greater than in controls exposed to the same en-

vironment. The rheumatic children appeared to be more susceptible to streptococcal infection than were controls. One injection of 300,000 units crystalline, 300,000 units procaine and 600,000 units benzathine, penicillin produced a rapid and marked fall in the streptococcal carrier rate, but oral penicillin, 200,000 units daily, proved ineffective.

A. B. Christie

HWANG, Wan & MA, Wan-Sen. **Rheumatic Heart Disease. A Resumé of Chinese Medical Association Symposium.** *Chinese Med. J. Peking.* 1960, May, v. 80, No. 5, 417–27, 1 chart.

BACTERIAL INFECTIONS

The order in this section is:—*General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.*

BOWLER, D. P. **Post-Diphtheritic Polyneuritis with Respiratory Paralysis.** *Med. J. Australia.* 1960, May 7, v. 1, No. 19, 733–4.

This is a report from Malaya of a case of diphtheria, in a Chinese child of 2½ years, undiagnosed and untreated in the acute stage, and observed throughout the stage of peripheral nerve paralysis from the 8th week onwards. It should make useful reading for those with little or no experience of diphtheria. There was evidence of paresis of the cranial nerves IX and X but not of III, IV, V, VI, or VII and also of many spinal nerves. This resulted in respiratory weakness with some accumulation of naso-pharyngeal secretions, and also in hypertension and semi-coma probably resulting from hypercapnia. Treatment with tracheotomy and intermittent positive pressure respiration rapidly brought about improvement. This treatment was maintained for 2 weeks and thereafter the child improved slowly without the respirator, but 3 months after admission all his tendon reflexes were still absent. [In this case the patient was fortunate to escape the early and most fatal complication of diphtheria—myocardial failure—which, however, is rare under 3 years of age. It should be recognized that it is only the late complication of polyneuritis that is described here.]

H. Stanley Banks

SELL, Sarah H. W., with the technical assistance of Frances C. WOMACK. **Some Observations on Acute Bronchiolitis in Infants.** *Amer. J. Dis. Children.* 1960, July, v. 100, No. 1, 7–15, 1 fig. [31 refs.]

This is a description of a carefully planned comprehensive study to evaluate the causal role of bacterium and virus in acute bronchiolitis of infants.

73 children all under 2 years were included. All had been ill with mild respiratory symptoms before the acute onset of severe respiratory distress. Naso-pharyngeal

secretions were examined for the presence of *Haemophilus influenzae* and *Streptococcus pneumoniae*. When the former organism was isolated it was typed. Antibody in the patients' serum was titrated by a capsule swelling technique and by an agglutination test.

Similar material from 48 of the patients was examined for the presence of virus in tissue culture. Serological virus studies were subsequently performed on the whole series of 73 cases.

H. influenzae was isolated from 48 (66%) of the 73 patients. Typable strains, mostly a and b were identified in 35 (48%). *Str. pneumoniae* was isolated from 21 (30%) either alone or in combination with *H. influenzae*.

Antibody to *H. influenzae* was identified in 68 (93%) and 59 (84%) respectively by the capsule swelling and agglutination tests. Only one patient had a rising titre of influenza A virus antibody although all sera were screened in addition for antibody to the following viruses; influenza A', B, C and swine and parainfluenza 1, 2 and 3.

No cytopathic virus and no evidence for the presence of a haemadsorbing virus was found in any of the 48 infants after examination in HeLa and monkey kidney cultures for approximately 3 weeks. R. G. Sommerville

SELL, Sarah H. W. & SHAPIRO, J. L. **Interstitial Pneumonitis induced by Experimental Infection with *Hemophilus influenzae*. Intranasal Inoculation of Day-Old Mice with Cultures originally isolated from Infants with Acute Bronchiolitis.** *Amer. J. Dis. Children.* 1960, July, v. 100, No. 1, 16-22, 6 figs. [14 refs.]

The strains of *Haemophilus influenzae* which were isolated from infants acutely ill with bronchiolitis were inoculated intranasally into mice 1 day old. The organisms which were isolated from naso-pharyngeal cultures and which belonged to types a (1) and e (2) were preserved by freeze drying. They were subsequently inoculated either alone or in combination with a bacteria-free filtrate of the nasopharyngeal secretions from each child, and appropriate controls were included in the experiment. All mice were killed on the fourth day and their lungs were examined histologically.

The changes produced were characteristically the development of an interstitial pneumonitis involving bronchial and bronchiolar walls and the surrounding alveoli. *H. influenzae* was recovered from most of the inoculated animals and it was not possible to differentiate the type of organism used from the histological picture produced. The addition of the filtrate had no effect on the proportion of mice infected. The pathological changes produced in the animals were similar to those found in human infants dying of bronchiolitis caused by *H. influenzae*.

R. G. Sommerville

NEHAUL, B. B. G. **Infantile Diarrhoea in British Guiana. Bacteriological Findings.** *West Indian Med. J.* 1960, Mar., v. 9, No. 1, 51-4. [11 refs.]

"In a study of the findings on bacteriological investigation of infantile diarrhoea in British Guiana during a

period of 14 months in 1958-59, the agents were as follows:—

<i>Shigella sonnei</i>	38%
<i>Shigella flexneri</i> types	16%
<i>Salmonella coeln</i>	16%
<i>Escherichia coli</i> types	24%

of 76 positive results.

"Deaths from diarrhoea represent some 22% of all deaths in infants aged one year and under."

KRANENDONK, O. [The Diarrhea of Travelers.] [Correspondence.] *Amer. J. Trop. Med. & Hyg.* 1960, Sept., v. 9, No. 5, 536-8, 1 fig.

This correspondence is about a recent paper on the diarrhoea of travellers [this *Bulletin*, 1960, v. 35, 264; see also 1959, v. 34, 206]. The authors of that paper considered that the enteropathogenic *Escherichia coli*, *Paracolobactrum* and *Klebsiella* isolated from students in that enquiry could not be incriminated as the cause of the diarrhoea of travellers to Mexico. The writer of the first letter in this correspondence considers that the results of the investigation recorded in that interesting paper when submitted to his further analysis of the data do provide some evidence that these organisms may be pathogenic. This evidence is (1) statistical analysis showed that the probability that the greater frequency of isolation of pathogens from the sick than from the healthy students could be due to mere chance is less than 5% and (2) on rearrangement of the data it was found that the reporting of diarrhoea shows a bimodal distribution during the period of observation. Pathogenic *E. coli* were isolated only within the first 9 days after arrival. On the 11th day no case of diarrhoea was mentioned but after this a second wave of diarrhoea occurred in which period *Paracolobactrum* and *Klebsiella* were "predominantly cultured". A table and a figure set out these findings.

It is realized that this analysis merely shows a statistical relationship between 2 phenomena but nevertheless indicates that the isolated enteric pathogens may be responsible for diarrhoea among travellers to Mexico.

In the second letter B. H. KEAN, one of the authors of the original paper recommends the publication of the analysis which he describes as "astute and provocative".

M. E. Delafield

HOEKENGA, M. T., CARRIZO, P., H. & GREEN, W. E. **Treatment of Severe Infectious Diarrhea in Infants with Colistin Salts.** *Antibiotic Med.* New York. 1960, May, v. 7, No. 5, 314-19.

Acute infective diarrhoea is the commonest cause of mortality in early childhood in western Panama, where the authors work in a hospital belonging to the United Fruit Company. The type of infection cannot always be determined, for *Shigella* and *Salmonella* types are rare. *Entamoeba histolytica* is very uncommon. In 95% of patients *Aerobacter aerogens*, *Pseudomonas pyocyanea*, *Escherichia coli* and other common enteric bacteria are isolated. Facilities for the recognition and typing of enteropathic strains of *E. coli* were not available, nor could a virological investigation of the stools be carried out.

In a search for more efficient antibiotic agents the authors have carried out a clinical trial of colistin, derived from a soil micro-organism *Aerobacillus colistinus*. This antibiotic is stable and can be prepared in a crystalline form; it appears to be free from toxicity and has a wide spectrum of activity against Gram-negative organisms, and is also effective against some Gram-positive bacteria. It is prepared in two forms, as the sulphate for oral use and as sodium colistin methanesulphonate for parenteral use. The oral dose is 5 mgm. per kgm. body weight in divided doses each 24 hours: for parenteral use the dose is calculated as 1.66 mgm. per kgm. per 24 hours (the dosages given refer to the base).

A clinical trial was carried out on 50 children acutely ill, toxic and dehydrated as a result of infective diarrhoea, 24 children received oral colistin, in 26 vomiting necessitated parenteral as well as oral administration. Stool culture revealed *Aerobacter aerogenes*, *Ps. pyocyanea*, coliforms, and in 1 instance each *Salmonella paratyphi B*, *Proteus mirabilis*, a coagulase-negative staphylococcus and *Shigella dysenteriae*. On disc testing, all the predominant organisms were sensitive to the antibiotic except the *Salmonella paratyphi B* and the *Shigella dysenteriae* [in the case of *Salm. paratyphi B* this does not seem to be clear from the Table].

The effects of treatment were judged as follows: excellent if stools returned to normal frequency and consistency in 48 hours, apparent cure if 72 hours were required for improvement, and satisfactory if recovery occurred within 96 hours: failure was recorded if marked improvement had not occurred after 96 hours treatment. Of the 24 children who received oral colistin all were cured in an average time of 3.4 days, the individual classification of the effect being excellent in 6, good in 13, satisfactory in 5. Of the more severely affected children who required parenteral treatment, 20 out of 26 were cured and there were 6 failures: the average time lapse before cure being 3.6 days. The results were classified as excellent 4, good 12, satisfactory 4, failed 6.

Rehydration by parenteral fluid administration was given along the accepted lines. There were no side effects of the drug, which appeared both effective and safe. [This new antibiotic appears promising but further clinical trials in infections with *Salmonella* and *Shigella* infections are clearly indicated.]

The results are tabulated and 6 case-histories are given.

J. H. Walters

RANDRIAMBOLOLONA, R. & DODIN, A., with the technical collaboration of E. RAKOTONDRA MANGA. Étude de l'évolution de la bactériémie dans onze cas de salmonellose traités. [Studies on Bacteraemia in Eleven Cases of Treated Salmonellosis] *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 278-85, 5 figs.

This paper is concerned with quantitative studies of the bacteraemia in patients suffering from typhoid fever by counting the actual numbers of typhoid bacilli in a measured quantity of blood taken from the patients. Normally when the bacterial count in the blood falls to zero the temperature of the patient subsides. If the temperature remains elevated it usually indicates a complication of the

disease itself or some other factor. In either case the bacteraemia curve offers information of value to the physician with regard to the progress of the patient.

The technique employed by the author is the membrane filter method whereby measured quantities of blood are filtered through specially prepared membranes which are then used directly as culture plates and the number of colonies of typhoid bacilli developing in the membrane will enable the number of typhoid bacilli per ml. blood to be estimated. The author does not claim that the method is superior to the classical techniques for blood culture, but he shows that it is equally reliable. Moreover it yielded results, which included the number of enteric organisms present in the sample, that were usually available 48 hours in advance of those obtained by the classical methods.

H. J. Bensted

HALAWANI, A., ABDALLA, A. & BADRAN, A. The Relation between Schistosomiasis and the Urinary *Salmonella* Carrier State. *Amer. J. Trop. Med. & Hyg.* 1960, July, v. 9, No. 4, 371-3. [11 refs.]

The urinary salmonella carrier appears to be much commoner among the Egyptian population than in populations in other parts of the world. This fact was recognized many years ago by bacteriologists working in Egypt but little was published until the surveys of Egyptian villages were undertaken by MILLER (*J. Egyptian Pub. Health Ass.*, 1950, v. 25, 45) and WEIR *et al.* (*ibid.*, 1952, v. 27, 55). Later MILLER and FLOYD [*this Bulletin*, 1954, v. 29, 803] drew attention to the possible connexion between urinary carriage of the enteric organisms and urinary schistosomiasis.

The present paper is concerned with a study of 3 groups of urinary enteric carriers under treatment with chloramphenicol. Group I consisted of chronic urinary carriers without evidence of schistosomiasis who received the antibiotic in doses of 3 gm. daily for 2 weeks. Group II were suffering from urinary schistosomiasis also; they were given the same treatment. Those failing to respond to the chloramphenicol were then actively treated for schistosomiasis and later re-treated with chloramphenicol. Group III were, like Group II, chronic urinary enteric carriers suffering from urinary schistosomiasis. These were first treated for the worm infection and when the urine was completely free from ova the chloramphenicol treatment was started. The standard of cure for the carrier state was negative cultures for a minimum of 6 weeks after the cessation of treatment. The bacteriological examinations of the carriers were carried out at weekly intervals [details are not given but it is presumed that none was an intermittent carrier]. There were 16 typhoid, 16 paratyphoid A and 4 paratyphoid B excretors. In Group I 10 out of 12 had ceased to excrete the organism at the end of the 6-week period; there were 2 relapses at 3 and 4 weeks respectively. In Group II 6 out of 12 responded to chloramphenicol, but 6 failed to respond until after the schistosomiasis had been successfully treated; they were then cured of their carrier condition with the second course of chloramphenicol. In Group III all the patients responded to the antibiotic, which was not started until they were cured of their schistosome infection.

H. J. Bensted

TURK, D. C. **Shigellosis and Sulphonamides.** *Lancet.* 1960, Aug. 27, 460-61. [14 refs.]

The author, writing of his experience of bacillary dysentery in Jamaica, draws attention to, what he calls, the world-wide increase in shigella strains resistant to sulphonamides and antibiotics. He, himself, has been particularly concerned with the sulphonamide-resistance of *Shigella sonnei* (22 of 24 strains).

[The very high proportion of sulphonamide-resistant cultures of *Sh. sonnei* among the total isolation tested is a common experience of clinical bacteriologists and much of this has not been published. But it is difficult to provide reliable figures about the development of resistant strains. Sonne dysentery is a very common disease in Great Britain and many other countries, probably much more common than official figures indicate, for much of it is of a trivial nature, of short duration and often overlooked. The fact that the clinical disease has so frequently cleared up before any treatment has been started and the fact that excretion of the organism may continue long after the cessation of any clinical sign make it difficult to assess the therapeutic value of any specific form of treatment. But it is the high infectivity of the long-term excreter, or convalescent carrier, that makes Sonne dysentery so important epidemiologically; the disease itself, except in the young infant, is rarely serious.]

Whether the sulphonamide-resistance of *Sh. sonnei* has or has not greatly increased in the post-war years it is important to remember that in the earliest days of sulphonamide treatment of bacillary dysentery the dramatic response to this group of drugs was seen with the Flexner infections, not the Sonne infections and resistant strains of *Sh. sonnei* were not uncommonly found in Great Britain during the war years when Sonne dysentery was still a relatively infrequent disease.

The epidemiological pictures of Flexner and Sonne dysenteries are usually distinct even in tropical and sub-tropical countries and it is unfortunate that in many accounts dealing with the incidence of bacillary dysentery the general term shigellosis is commonly used when it would be valuable to know more precisely the types of organisms involved.]

This short paper raises a number of interesting problems.

H. J. Bensted

TISHCHENKO, I. T., SMOGARZHEVSKAIA, I. E., SOFIENKO, N. I., KONSTANTINOVA, A. A. & LUR'E M. A. **The Aetiology and Epidemiology of Intestinal Dysfunctions caused by Pathogenic *Escherichia coli*.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 12, 132-5. [Translated from Russian.]

The observations recorded here in respect of infantile enteritis are mostly in accord with the numerous published accounts of epidemiological studies of this disease in different parts of the world where the "pathogenic coli" appears to be the cause of the condition. This report comes from the Kiev area where *Escherichia coli* O 111 is the commonest type of the pathogenic coli isolated. O 55 and O 26 are much less common. In a small-scale investigation the authors found a specific agglutinin res-

ponse to the infecting strain of organism. While it is considered that the infection is due to exogenous spread, it is felt that the endogenous route should not be dismissed. The disease was of particular importance in infants under 1 year and the peak incidence was in the autumn and winter months, although cases occurred throughout the year.

H. J. Bensted

LINDE, K., KÖDITZ, H. & FUNK, G. Die Mehrfachinfektionen mit Dyspepsie-Coli, ihre Beurteilung in statistischer, bakteriologischer und klinischer Sicht. [Mixed Infections with Pathogenic *Escherichia coli*] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 1, 94-108. [52 refs.]

The importance of mixed infections of different kinds is here considered from the epidemiological and synergic viewpoints to introduce the statistical, bacteriological and clinical observations recorded in this paper.

A table sets out the results of bacteriological findings in respect of positives for pathogenic *Escherichia coli* in the examination of about 10,500 faecal specimens in the years 1954-59 in Jena. The totals of types O 111, O 55 and O 26 which were isolated, and the frequency of double infections with these types (there was one triple infection), are given. The data were analysed, by a statistical method which is described, to determine the expectation of a mixed infection and hence compare this with the observed experience. Statistically significant differences between expectation and observation were very infrequent, but when they occurred they suggested the introduction of some particular epidemiological or clinical factor.

Some further work was done on mixed infections of these types with *Salmonella*, *Shigella* and *Pseudomonas pyocyanea* and this is also described and discussed.

M. E. Delafield

KELLY, P. J., MARTIN, W. J., SCHIRGER, A. & WEED, L. A. **Brucellosis of the Bones and Joints. Experience with Thirty-Six Patients.** *J. Amer. Med. Ass.* 1960, Sept. 24, v. 174, No. 4, 347-53, 3 figs. [18 refs.]

Of the 36 patients reviewed, 22 were suffering from culturally confirmed brucellosis, the remaining 14 showed agglutination titres in the serum to a dilution of at least 1:800. The authors note, however, that only 5 of those culturally confirmed showed titres of 1:800 or higher and therefore conclude that, in choosing this titre, other cases of orthopaedic brucellosis must have been excluded. Nevertheless, with lower titres, there is no certainty that the lesions are brucellar in origin.

One patient yielded a positive blood culture, other positive cultures were obtained chiefly from tissue culture as fluid from joints or pus from discharging sinuses may fail to yield a *Brucella* when it can be grown from the affected tissue. Prepatellar bursitis was a relatively common manifestation, being present in 8 of the 22 culturally confirmed. Brucellar osteomyelitis showed no radiographic changes peculiar to brucellosis. Saucerization of bony lesions was found to be necessary and secondary

infection by other pyogenic organisms was prone to occur. Brucellar spondylitis was a frequent lesion, especially in the group not confirmed by culture, and in a number of instances the first diagnosis had been a suspected "slipped disc". A paravertebral abscess was noted in 2 patients. The authors found that, except for spondylitis, active surgical treatment was usually required, including excision of synovial tissue. They found tetracycline and streptomycin given for 4 weeks generally successful. Some patients were treated with streptomycin and sulphadiazine. [No observations appear to have been made on the use of the 3 drugs simultaneously and a comparison between conservative and surgical treatment is not presented.]

The organisms cultured were *Brucella abortus* (8), *Br. suis* (8), *Br. melitensis* (4) and in 2 the species was not determined [the table shows 9 *Br. abortus* and 1 unidentified]. The incidence was almost entirely in males associated with farming or meat handling.

[A valuable and well illustrated report. The authors would do well to read the classical description of J. A. MARSTON (1863) Army Medical Reports for 1861, rather than to rely on an inaccurate quotation.]

Frederick J. Wright

PARNAS, J., ZWOLSKI, W., ŁAZUGA, K., KOSLAK, A., UMINSKI, J. & BURDZY, K. O badaniach zoologicznych, mikrobiologicznych i parazytologicznych w czasie ekspedycji organizowanych dla opracowania ognisk naturalnych antropozoonoz. [Zoological, Microbiological and Parasitological Investigations during the Expeditions organized for Exploration of Natural Foci of Anthroozoonoses] *Wiadomości Parazytologiczne*. Wrocław, 1960, v. 6, Nos. 2/3, 125-40, 1 fig. [27 refs.] English summary.

In 1953 and again in 1955-59 field investigations were carried out in foci of leptospirosis and brucellosis in the Polish provinces of Lublin and Szczecin. 3358 small mammals and birds were caught and identified, and the frequency of the different species is shown in a table. The ectoparasites living on 1,679 animals were also identified; attempts to isolate leptospires and *Brucella* spp. from them were unsuccessful. In laboratory investigations no leptospires could be isolated from larvae and nymphs of *Ixodes ricinus* fed on guinea pigs, mice and common voles artificially infected with *Leptospira grippityphosa*. *Brucella abortus* could be recovered from *Hoplopleura acanthopus* fed on artificially infected common voles, and lice could therefore act as vectors of brucellosis in natural conditions.

D. J. Bauer

ADDAMIANO, L., BABUDIERI, B., BUSSINELLO, E., GIUSTI, G. & SALVI, A. Ricerche ed indagini sperimentali sulle leptospirosi degli uccelli. Loro importanza epidemiologica. [Research and Experimental Studies on Leptospirosis in Birds] *Rendiconti Istituto Superiore di Sanità*. Rome, 1960, v. 23, Pt. 5, 482-96, 3 figs. [31 refs.]

"A high percentage of marsh birds captured in the Vercelesse rice fields showed the presence of leptospira

in their organs especially the liver and kidney. When these could be obtained in pure culture they proved to belong to *L. bataviae* serotype—the most common agent of leptospirosis in the Italian rice fields.

"It is possible to infect young waders and domestic ducks both by subcutaneous injection and orally.

"The leptospira can be grown for some days from the blood of these birds.

"The agglutinins often appear in significant titre in the blood but rapidly disappear again.

"Some of the experimentally infected birds become carriers and eliminate pathogenic leptospira through the cloaca even for some months. It is possible that these birds, which are almost all migratory, have importance in carrying pathogenic leptospira from infected regions to others which were previously free."

BREWER, W. E., ALEXANDER, A. D., HAKIOGLU, F. & EVANS, L. B. Rice-Field Leptospirosis in Turkey. A Serologic Survey. *Amer. J. Trop. Med. & Hyg.* 1960, May, v. 9, No. 3, 229-39, 1 fig. [26 refs.]

The cultivation of rice frequently provides optimum conditions for the spread of leptospirosis in man and animals.

The present study deals with the South Central region of Turkey, that part located at the eastern end of the south coast near to Syria, between the Taurus mountains and the Mediterranean Sea. The region was arbitrarily divided into 4 areas, based roughly on the number of years in rice production: area I, 10 years; II, 60 years; III, 300 years; IV, where rice is not grown but which is devoted to improvement of livestock-breeding and agricultural techniques.

Men, women, and children from the local villages carry out the cycle of planting, weeding, and harvesting; and, unlike the practice in Italy, few migratory workers are brought in to help.

The soil is very moist at planting time, is inundated later, and still contains muddy patches and small water holes at harvest time. The pH of the rice-field water varies between 6.2-8.0; the pH of the streams is 7.2.

Cattle from each village are kept in a common herd while grazing during the day and are returned to their owners before nightfall. Sheep and goats may or may not be herded together and returned to the village each night. Horses and donkeys, used mainly for riding, are kept near the village.

In each area, sera were obtained from human beings and domestic animals at villages which were selected without bias. The sera were screened in a microscopic agglutination (-lysis) test with living suspensions of 18 serotypes of leptospires. Reactions were considered to be positive when 75% of the organisms were agglutinated or "lysed" at dilutions of 1 in 100 or higher: a very conservative criterion.

The prevalence of seropositive reactors, human beings and domestic animals, varied considerably between villages in each area; but it could not be related to the practice of rice cultivation or to its duration. Moreover analysis of the distribution of serological titres in cattle, goats, and sheep indicated that outbreaks of leptospirosis had recently occurred or were in progress at the time

of survey. The overall prevalence of seropositive reactors in the region was: human beings, 9.6% (23/240); cattle, 59.0% (539/914); goats, 63.3% (69/109); sheep, 22.4% (11/49); horses, 47.8% (55/115); donkeys, 58.0% (29/50).

The determination of infecting serotypes on the basis of host serological response can only be presumptive [ALEXANDER *et al.*, this *Bulletin*, 1958, v. 33, 702]; but among the 726 positive sera they appeared to be principally *Leptospira grippityphosa* (250) and a member of the *hebdomadis* group, possibly *L. sejroe* (352). The predominant titre in other sera was elicited with *L. autumnalis* in 32, *L. andaman* 8, *L. semarang* 8, *L. australis* 3, *L. bataviae* 2, *L. pyrogenes* 1, and with *L. ballum* in 1. In addition, reactions to the same titre with 2 or more serotypes were obtained in 69 sera (*grippityphosa*+*sejroe*, 46).

In human beings, goats, and sheep most of the predominant positive reactions were elicited with *L. grippityphosa*. In cattle, however, the predominant reactions were as follows: with the *hebdomadis* group, 328; *grippityphosa*, 139; multiple and others 72. In equine sera the distribution was more or less even among *grippityphosa*, *hebdomadis*, *autumnalis*, and multiple reactions.

The findings of this study differ from those in rice-field areas of other Mediterranean countries primarily as regards the prevalence and types of antibodies found. The prevalence in human beings (9.6%) was lower than that reported in other areas; but slight relaxation of the criterion to include sera showing 50–75% agglutination would give the rate as 32% which is more comparable.

Human leptospirosis in other Mediterranean rice-field countries is primarily associated with migrant workers and areas newly converted to rice-growing; and the protean, often mild, clinical manifestations are well known. These 3 factors probably account for the fact that human infections in the Turkish rice areas have not been particularly noted. The step-wise increase in the percentage of seropositive reactions with increased age, as reported in other studies, was not observed; the reason may be that infections are acquired at an early age and residual antibodies decrease below detectable levels over the ensuing years. Rodents of species known to carry *L. grippityphosa* and *L. hebdomadis* occur in these areas but were not studied in this survey.

[Useful references to the subject of leptospirosis in rice-field workers are given. See also this *Bulletin*, 1957, v. 32, 753, 953.]

L. H. Turner

BRACHMAN, P. S., PLOTKIN, S. A., BUMFORD, F. H. & ATCHISON, Mary M. **An Epidemic of Inhalation Anthrax: the First in the Twentieth Century. II. Epidemiology.** *Amer. J. Hyg.* 1960, July, v. 72, No. 1, 6–23, 8 figs. [26 refs.]

During a 10-week period in 1957 5 cases of inhalation anthrax and 4 cases of cutaneous anthrax occurred in a New Hampshire goat hair processing mill. No case of inhalation anthrax had previously been reported at this mill and analysis of death certificates and other health records did not suggest that any such cases had been missed. Cutaneous anthrax on the other hand was a known occupational risk and 136 cases had occurred in 6½ years.

As expected, the disease affected workers employed on dusty and dirty jobs—4 of the 5 patients with inhalation anthrax worked in combing or carding processes. Serological and autopsy studies revealed nothing which might be regarded as a precipitating factor: a percentage of sera positive to Q fever, higher than in the general population, was shown to have been present in previous years: the percentage positive to adenovirus and to influenza virus did not differ from the normal population percentage and there was no clinical evidence of any respiratory illness among the workers at the time of the anthrax epidemic.

A trial of anti-anthrax vaccine had been carried out earlier in the year and, although none of the anthrax patients had been vaccinated, it was not possible to conclude that the vaccination state of the workers had any bearing on this outbreak, although the authors feel that, when experience elsewhere is considered as well, it can be claimed that vaccination is effective. Air sampling showed that a worker in the carding room might inhale between 600 and 2,150 anthrax-bearing spores per 8-hour shift, of which 150–700 were less than 5 microns in diameter—the size of particle which can reach the alveoli of monkeys. Antibody studies suggested that 33% of workers in the carding and combing rooms had been infected subclinically with anthrax and such infection may well have protected some workers. 50% of goat hair entering the factory was shown to be infected with anthrax bacilli but less than 5% of swabs from surfaces in the mill were positive. A consignment of goat hair from India, shown to be more highly contaminated than usual, was associated in time with the outbreak. A new detergent process, shown experimentally to enhance the virulence of anthrax bacilli, had also been introduced just before the outbreak but could not have been concerned in the first case.

The full explanation of the outbreak remained obscure. [This is an article of unusual importance to anyone interested in anthrax.]

A. B. Christie

DAHLGREN, C. M., BUCHANAN, L. M., DECKER, H. M., FREED, S. W., PHILLIPS, C. R. & BRACHMAN, P. S. **Bacillus anthracis Aerosols in Goat Hair Processing Mills.** *Amer. J. Hyg.* 1960, July, v. 72, No. 1, 24–31, 2 figs. [21 refs.]

Air sampling was carried out in 2 mills in Pennsylvania and in New Hampshire after the outbreak of inhalation anthrax in the latter mill. Anthrax bacilli formed only 0.1% of the total number of organisms in the air of the weaving departments and 0.9% in carding rooms. The findings in the 2 mills were very similar and gave no explanation of the epidemic at the New Hampshire mill. In the carding rooms between 620 and 2,200 anthrax particles could be inhaled in 8 hours by a non-immune individual: of these particles between 140 and 690 would be under 5 microns in diameter and capable of reaching the alveoli. The figures suggest that great variation can occur from time to time in the number of anthrax bacilli in the air of the same department but do not exclude the possibility that some factor other than numbers of bacilli in the air may be responsible for the onset of inhalation anthrax.

A. B. Christie

NORMAN, P. S., RAY, J. G., Jr., BRACHMAN, P. S., PLOTKIN, S. A. & PAGANO, J. S. **Serologic Testing for Anthrax Antibodies in Workers in a Goat Hair Processing Mill.** *Amer. J. Hyg.* 1960, July, v. 72, No. 1, 32-7. [14 refs.]

A serological survey of workers in the New Hampshire mill after the outbreak of anthrax showed that of 72 unvaccinated workers 11 had sera positive to anthrax: 7 of the 11 worked in the area of the mill where 6 of the 9 cases of anthrax occurred. This suggests subclinical infection but it is not possible to decide whether infection took place at the time of the epidemic or earlier. Some figures suggest that antibody titres fall rapidly—18 of 33 vaccinated workers had negative titres 6 months after vaccination and 1 of the workers who had a positive titre in 1953 had a negative titre in October 1957 but a positive in November 1957. Positive sera in normal populations were rare.

A. B. Christie

KUKIZ, T. & MIKULSKI, Z. Teżec w Polsce na tle sytuacji światowej. [**Tetanus in Poland on the Background of the World Situation**] *Przegląd Epidemiol.* Warsaw. 1960, v. 14, No. 2, 117-26, 5 figs. [25 refs.] English summary.

The mean tetanus mortality between 1951 and 1956 in Poland was 117 per 100,000, a figure which was exceeded in Europe only in Yugoslavia and France. According to the statistics for 1946-57, 75% of the cases occurred between May and October. The provinces of Rzeszów and Crakow were mainly affected. An analysis of the incidence and mortality according to age is presented for 1954-57, based in part on a questionnaire issued by the Ministry of Health in 1956-57 covering 627 cases. Infants up to 1 year of age were mainly affected (26.94% of all recorded deaths in 1954-56 and 14.44% in 1956-57); 380 (60.6%) of the cases recorded in 1956-57 were in males, and 80% occurred in rural areas. The case mortality in the latter period was 46%.

D. J. Bauer

TALSTAD, I. Tetanus behandlet med meprobat. [**Tetanus treated with Meprobat**] *Nordisk Med.* 1960, Oct. 27, v. 64, No. 43, 1353-5, 1 fig. [18 refs.]

The English summary appended to the paper is as follows:—

"A report is presented on a case of grave tetanus which was treated successfully with tracheotomy and meprobat intramuscularly."

LEWANDOWSKI, A. Własne spostrzeżenia nad leczeniem ciężkich postaci żeńca mieszanką lityczną, kurarą i ciągłym oddechem kontrolowanym. [**Treatment of Severe Forms of Tetanus with Lytic Cocktail, Curare, and Continuous Controlled Respiration**] *Przegląd Epidemiol.* Warsaw. 1960, v. 14, No. 2, 163-9. English summary (8 lines).

The author reports the results of the treatment of 13 patients suffering from tetanus in 1957 in Poznan, Poland,

with lytic cocktail (largactil, dolantin and phenergan in doses corresponding to the severity of the illness), curare and continuous controlled respiration with mechanical or hand apparatus. Tracheotomy was carried out in 10 instances. Recovery was obtained in 5 of 7 severe cases with an incubation period of 7-18 days and in 3 of 5 very severe cases with an incubation period of 4-8 days. Death occurred in a child aged 8 years who developed tetanus fulminans after an incubation period of 4 days.

D. J. Bauer

LISSNER, Maria. Leczenie żeńca mieszanką lityczną. [**The Treatment of Tetanus with Lytic Cocktail**] *Przegląd Epidemiol.* Warsaw. 1960, v. 14, No. 2, 171-3. [14 refs.] English summary.

Between 1956 and 1959, 26 patients suffering from tetanus in Lodz, Poland, were treated with a mixture of 25 mgm. each of largactil and phenergan and 50 mgm. of dolantin given intravenously twice daily dissolved in saline, together with tetanus antitoxin, antibiotics and other measures; 13 recovered. In 9 patients treated in the latter part of 1959 the doses were doubled and 0.22 gm. of luminal was also given intramuscularly, together with antiserum; 7 recovered and the remaining 2 died within 24 hours of admission to hospital.

D. J. Bauer

KANIAK, J., CYWICKI, J. & SMOLENSKA, Wiesława. Próba oceny skuteczności leczenia żeńca na materiale szpitali zakaznych Dolnego Śląska. [**Attempts to Evaluate the Efficacy of Tetanus Treatment from the Material of the Infectious Disease Hospitals in Lower Silesia**] *Przegląd Epidemiol.* Warsaw. 1960, v. 14, No. 2, 177-81. [18 refs.] English summary (8 lines).

Between 1949 and 1950, 230 patients suffering from tetanus were treated in hospitals in Lower Silesia; 9 cases were very severe, 123 severe and 86 moderate, with mortalities of 100%, 57% and 7.3% in the 3 categories respectively. The remaining 12 patients suffered from a mild form of the disease and all recovered. There were 86 deaths (36%). 218 patients were treated with antiserum and with hypnotics, largactil, prednisone, insulin and antibiotics in various combinations. The lowest mortalities (2 of 9 cases, 22%; 5 of 26 cases, 19%) were observed with insulin treatment combined with hypnotics.

D. J. Bauer

FORDE, H. McD. & WILLIAMS, H. M. **Tetanus in Barbados.** *West Indian Med. J.* 1960, Mar., v. 9, No. 1, 9-13.

This is a brief review of 29 cases of tetanus treated in Barbados General Hospital between August 1957 and July 1958. 17 of the patients were under 19 years of age and 10 were over 40. 8 patients died, 5 being under 15 and 3 over 40 years of age. Standard treatment was antitetanic serum—only 1 patient had less than 70,000 units—sedation by sodium amylal or sodium phenobarbitone and chlorpromazine.

A. B. Christie

HOUSTON, A. N., ROY, W. A., FAUST, R. A. & EWIN, D. M. **Tetanus Protection.** *Southern Med. J.* 1960, June, v. 53, No. 6, 700-705.

This paper does not contain any account of original investigations on the subject of prevention of tetanus but is more in the nature of a plea for a national campaign in the United States for general immunization against tetanus by means of tetanus toxoid. Full consideration is given to the importance of adequate surgical cleansing and débridement of wounds in all cases of tetanus-prone injuries and this is followed by a guide to further treatment. The dangers of antitoxin as a routine measure are stressed although the use of combined active and passive prophylaxis is accepted for special cases, but detailed instructions about dosage in such cases are not given.

[The general statements are sound but the paper is too superficial to be regarded as anything much more than useful propaganda for active immunization against tetanus.]

H. J. Bensted

CLAYPOOL, B. W., JR., WELLMAN, W. E., NEEDHAM, G. M. & ACHOR, R. W. P. **Listeria monocytogenes Meningitis: Brief Review of the Literature and Report of a Case.** *Proc. Staff Meetings Mayo Clinic.* 1960, Oct. 12, v. 35, No. 21, 609-14, 1 fig. [12 refs.]

VIRUS INFECTIONS

The order in this section is:—*General Psittacosis-Lympho-granuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.*

MATUMOTO, M., OMORI, T., OGATA, S., KURIHARA, H. & OKAMURA, R. Apparition des anticorps contre le virus de la psittacose chez les sujets humains expérimentalement infectés avec le virus de la conjonctivite à inclusions. [Appearance of Antibodies to Psittacosis Virus in Persons Experimentally Infected with the Virus of Inclusion Conjunctivitis] *C.R. Soc. Biol.* 1960, v. 154, No. 4, 890-92, 1 fig.

This paper records the production of antibody for psittacosis virus in 3 adult human subjects by infecting them with the virus of inclusion conjunctivitis. Antibody was measured by complement-fixation and by the inhibition of haemagglutination. The sera of all 3 were devoid of such antibody before infection; good titres were obtained in 2 but the response in the third was less good.

[No attempt apparently was made to show whether or not these antibodies were reacting solely with the group antigen in psittacosis virus. Presumably there were psittacosis-lymphogranuloma group antibodies.]

S. P. Bedson

DEODHAR, N. S. & DONGRE, P. M. **Smallpox within Nine Months of Primary Vaccination. A Case Report.** Reprinted from *Indian Med. J.* 1960, Sept., 199-200, 3 figs. on pl.

The child was vaccinated at the age of 3 months. A photograph showing the presence of two scars on the left upper arm testifies to the success of the operation. At the age of one year, after a few days fever, the child developed a sparse rash on the upper and lower limbs with a few lesions on the face but none on the trunk. Many of the lesions aborted: a few progressed to scab formation. In the ordinary course such a mild case would never have been reported [in India] as even a suspected case of smallpox, but in this event the mother was living in the same compound as the local Infectious Diseases Hospital and 2 weeks before the child's illness had herself been attending a case of smallpox.

The "smear test" done on the 2nd day of admission was found "to accord the diagnosis". Revaccination failed to "take".

Two photographs, each of a part of the child's body, show some fleshy papular lesions on the left thigh and on the buttocks.

[The abstracter would not readily accept the diagnosis of smallpox solely on the evidence presented in this report.]

J. Pickford Marsden

KEMPE, C. H. **Studies on Smallpox and Complications of Smallpox Vaccination.** E. Mead Johnson Award Address. *Pediatrics.* Springfield, Ill. 1960, Aug., v. 26, No. 2, 176-89, 15 figs. (12 coloured).

It is well recognized that it is sometimes difficult to vaccinate [successfully] the very young child. Study of the haemagglutination-inhibition antibody levels in the sera of 182 mothers and their newborn infants showed that significant levels of antibody against vaccinia had been passed and, furthermore, that in some 40% of the cases the level in the infant was even higher than in its mother.

2 infants who could not be vaccinated successfully because of high level of maternal antibody did react at the age of 6 months with modified reactions maximal on the 5th and 6th days respectively without any earlier sensitivity type of reaction. This suggested that the present reactions were examples of antibody-modified primary vaccinia.

Small-scale evidence from Madras, and more recently from England, suggests that a combination of the use of hyperimmune vaccinal gamma globulin and successful vaccination or re-vaccination may produce a better protective effect than successful vaccination alone in certain types of smallpox contacts [but much more field work on this aspect remains to be done]. Clinical smallpox does, of course, occur in patients bearing vaccination scars; but patients with smallpox who have been said to have been vaccinated shortly before known exposure have been shown to have had only the early allergic response which was misinterpreted as a "reaction of immunity".

Confirmation of the view that significant viraemia regularly occurs in uncomplicated primary smallpox vaccination was not obtained. Over 100 attempts to isolate virus from blood in such cases failed. On the other hand, in the author's opinion, the "antigenic mass" depends rather on the amount of cutaneous and subcutaneous virus multiplication.

Hyperimmune vaccinal gamma globulin was used in 300 patients—therapeutically in 62 cases of generalized vaccinia; in 132 of eczema vaccinatum; in 23 of vaccinia necrosum; in 12 of vaccinia encephalitis, and in 27 cases of auto-inoculation. The material was also used prophylactically in 44 instances either for passive-active immunization of children suffering from eczema and yet requiring vaccination; or in instances of severe burns or chickenpox in recently vaccinated children. In none of this last group did any virus spread occur. There was no evidence that in the cases of encephalitis the gamma globulin influenced the course of the disease for the better. The 27 patients with auto-inoculations did well. 2 brothers acquired identical lesions of the eye. The eye of the untreated brother required 4 weeks to heal and left some residual scarring of the cornea. The lesion of the eye in the antibody-treated brother subsided within 24 hours and left no scar. In a group of 132 cases of eczema vaccinatum there were 9 deaths, a mortality rate of 7%. This compares favourably with the 30 to 40% usually encountered in young children treated only by supportive measures.

62 patients suffering from "generalized vaccinia" received gamma globulin. This condition is described as a "complication [which] occurs in children who have perfectly normal skin and whose peripheral lesions must be assumed to be blood borne". The clinical course in this series was benign. The 23 cases of vaccinia necrosum (mortality rate 30%) included 2 with profound hypogammaglobulinaemia: these proved fatal in spite of massive antibody therapy. However, even agammaglobulinaemia *per se* does not necessarily lead to vaccinia necrosum.

It is puzzling that some antibody-deficient individuals with vaccinia necrosum respond dramatically to antibody administration; others have entirely uncomplicated vaccinations; and some with normal levels of gamma globulin in their serum, but unable to produce vaccinia antibodies, fail to respond when these antibodies are provided passively, even in huge doses. This suggests the need for a cellular defence mechanism in addition to humoral antibody formation, a view supported by the finding that children with agammaglobulinaemia and uncomplicated vaccination histories showed a prompt allergic response to vaccination with heat-killed vaccinia virus, whereas patients with vaccinia necrosum did not.

Finally, the author hopes to develop an immunologically satisfactory killed vaccine for use on eczematous infants which might even be used universally "as a basic sensitizing experience", thus making "subsequent immunization with live vaccinia virus perhaps completely safe for everyone".

[There is much in the views and the research described in this article which demands that it be studied in full.]

J. Pickford Marsden

ESSWEIN, J. G. & DiDOMENICO, V. P. **Hemorrhagic Varicella Pneumonia.** *Ann. Intern. Med.* 1960, Sept., v. 53, No. 3, 607-13, 3 figs.

A number of reports have appeared recently of pneumonitis in severe cases of chickenpox in adults: it has also been indicated that steroid therapy is likely to have a deleterious effect on the course of a varicella illness.

In the present case, which concerned an obese man aged 37, the illness started with chills, fever, and abdominal pain some 9 days before the rash (on which the diagnosis of varicella was made) appeared. Later this became generalized, pustular and haemorrhagic. Thereafter the dominant picture was of gross respiratory embarrassment with the expectoration of profuse blood-stained sputum. When the patient seemed to be in extremis he was given continuous oxygen, cortisone 100 mgm. 3 times a day, and tetracycline 250 mgm. every 4 hours.

The patient recovered. Serial chest X-rays show the development, and subsequent clearance, of infiltrates in the lower lung fields. White cell count rose from 12,900 to 22,200. From sputum "alpha streptococcus" and "*Staphylococcus aureus*" grew. A melaena stool passed may have provided evidence of gastro-intestinal bleeding or may have had its origin in swallowed sputum.

J. Pickford Marsden

MONTGOMERY, R. R. & OLAFSSON, M. **Waterhouse-Friderichsen Syndrome in Varicella.** *Ann. Intern. Med.* 1960, Sept., v. 53, No. 3, 576-9.

"A case of Waterhouse-Friderichsen syndrome in an adult with varicella is presented. The clinical course and the findings at autopsy confirmed the diagnosis."

LIPPI, M., CORSO, P. & FRUGONI, G. Contributo sieroimmunologico alla conoscenza delle principali virosi. Ricerca nei soggetti sani degli anticorpi devianti il complemento verso il virus della parotite epidemica. [Sero-immunological Contribution to the Knowledge of the Principal Virus Diseases. Investigation of Healthy Persons for Mumps Complement-fixing Antibody] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, June, v. 41, No. 6, 283-322, 2 graphs. [205 refs.] English summary (6 lines).

The authors have examined the sera of 372 healthy persons living in Rome for the presence of antibody fixing complement with a preparation consisting of mixed mumps V and S antigens purified from infected allantoic fluid by fluorocarbon treatment. The persons investigated were aged from 30 days to 80 years and had no history of mumps infection. At the time when the sera were obtained an epidemic of mumps was in progress. Antibody in titres of 4-16 was found in 165 sera (44.3%) but was not present in the sera of 40 infants aged up to 1 year. The highest proportion of positive results (39 of 59 sera, 66%) was found in those aged 5-19 years.

The paper begins with a lengthy review of the literature on mumps virus.

D. J. Bauer

GILL, E. Diagnostischer Hauttest bei Mumps. [Diagnostic Skin Test in Mumps] *Deut. med. Woch.* 1960, Aug. 19, v. 85, No. 34, 1504-6, 1516.

A mumps skin test antigen was prepared from the parotid glands of rhesus monkeys, infected with mumps virus, by suspension in saline and inactivation by heating at 65°C. for 20 minutes; 0.5% phenol was added as a preservative. An area of erythema 15 mm. in diameter or greater, which was regarded as a positive reaction, was produced on intradermal injection in 9 of 12 persons who had previously suffered from mumps. Of 10 patients suffering from mumps who were tested on the 2nd-4th days of illness 2 gave a weakly positive reaction (15 mm. in diameter) and the remainder gave a negative result; on reinvestigation on the 10th-14th days of illness an area of erythema exceeding 15 mm. was observed in 2 and of 15 mm. diameter in 6 patients.

D. J. Bauer

FINGER, G. & MÖBEST, H. Epidemiologie und Prophylaxe der Asia-Grippe 1957/58 in der Bundeswehr. [Epidemiology and Prophylaxis of Asian Influenza in the Armed Forces of Federal Germany] *Arch. f. Hyg. u. Bakt.* 1960, Oct., v. 144, No. 7, 519-34, 3 figs.

SIEGERT, R., ENDERS, G. & FALKE, D. Serologische Studie zur Epidemiologie der Influenza A₂. [A Serological Study of the Epidemiology of A₂ Influenza] *Arch. f. Hyg. u. Bakt.* 1960, June, v. 144, No. 4, 234-48, 3 figs. [34 refs.]

The authors have carried out serological investigations on 3 population groups in Germany during the epidemic of Asian influenza in the autumn of 1957. Among a group of 49 healthy institution inmates 72 years of age or over who had experienced the influenza pandemic of 1889-90 12 (24.5%) possessed A/Asia/57 complement-fixing antibody in a titre of 20 or higher, compared with 3 of 108 (2.8%) of a group of healthy persons aged 18-22 years. A titre of 20 was attained or exceeded in 6 patients suffering from virologically confirmed Asian influenza and in 210 patients diagnosed clinically, and this level was therefore taken as diagnostic in subsequent investigations. A rise in titre of A and A-prime antibodies was also observed, but 8 infants aged 1-2 years showed only a homologous response to infection, and it is pointed out that children of this age-group should form suitable subjects for ascertaining the type of virus responsible for an epidemic. The antibody response was also studied in 2 units of soldiers and frontier guards affected by the epidemic. In the first unit of 150 men 50 (40%) developed Asian influenza; a diagnostic rise in homologous titre developed in 54 of these, and also in 48 of the 90 men (53%) who did not fall ill. In the second unit of 102 men 71% developed clinically manifest illness, and the results of serological investigations indicated that 90% had undergone infection.

D. J. Bauer

DUXBURY, A. E. & KEEN, T. E. B. Study in the Efficiency of Vaccination against Influenza in Two Employment Groups in Melbourne in 1959. *Med. J. Australia.* 1960, Aug. 6, v. 2, No. 6, 260-8, 5 figs.

Two employment groups in Melbourne were vaccinated in the autumn of 1959 with a polyvalent influenza vaccine containing strains of Swine, A, A1, A2, B and Sendai virus. The next summer, December 1959, they filled in a form regarding their vaccination history and the number of respiratory illnesses, attacks of influenza and days off work during the year. Those who had received 2 doses of vaccine in 1959, or one in 1959 and 2 in 1958 were considered to be satisfactorily vaccinated; others were used as the control group. Laboratory data were available to indicate what viruses were current in the city at different periods. There was less "influenza-type" illness in the vaccinated populations of both groups during May when A2 influenza virus was frequently isolated from such cases. In one group there was a similar apparent protection in July when influenza B was not active and the haemadsorption virus type II (closely related serologically to Sendai virus) was first isolated in the city, where it persisted until the summer (December). The protection rate of 60% was thought to be lower than might have been found if vaccination had been started earlier, and the protection in July may have been due to the Sendai component of the vaccine.

[One might criticize the design of this experiment on a number of counts, e.g. the nature of the control group, the reliance on a questionnaire returned from an unstated proportion of the groups inoculated, the danger of reluctance to diagnose clinical influenza in persons known to have been vaccinated against the disease. Nevertheless the results presented for influenza A2 look reasonable and it is therefore possible that the apparent effect of the vaccine in July was due to the Sendai component. It is to be hoped that a further trial will confirm this previously unreported finding.]

D. A. J. Tyrrell

KAPIKIAN, A. Z., CHANOCK, R. M., BELL, J. A., REICHELDERFER, T. E. & HUEBNER, R. J. A Study of the Hemadsorption Viruses (Para-Influenzae) and other Viruses in Children with and without Respiratory Disease. *Pediatrics.* Springfield, Ill. 1960, Aug., v. 26, No. 2, 243-8.

The authors studied 155 patients, aged 2 months to 4 years, suffering from respiratory disease and 105 control patients with non-respiratory disease in hospital and in the outpatients' department of the District of Columbia General Hospital, Washington D.C., in the winter of 1957-58. Throat swabs from all patients were tested for viruses by tissue culture inoculation, and paired sera were collected from 41 patients and 13 controls and tested by complement-fixation tests. The second serum specimens were collected 3-8 weeks after the acute serum.

Parainfluenza virus type 1 or 3 was isolated from 7 respiratory disease patients and from no control patients; although adenovirus type 2 was found in the throats of 4 of each group. A rise in complement-fixing antibody against parainfluenza viruses (mainly type 1) was found

in 17 of 41 respiratory disease patients and 1 of 13 control patients. The authors suggest that some of the antibody rises were due to hospital infections not connected with the diseases. The final diagnosis of illness of patients with parainfluenza virus infections "included most of the common childhood nonbacterial respiratory diseases" from mild upper respiratory disease by way of bronchitis to pneumonia.

[The numbers of virus isolations in the study are small but the laboratory and clinical data have apparently been included in the account of the whole collaborative investigation which has been previously published [CHANOCK *et al.*, this *Bulletin*, 1958, v. 33, 621; 1959, v. 34, 730]. The numbers in the combined investigation were large enough to support the conclusions reached in the present report.]

D. A. J. Tyrrell

KENDALL E. J. C., COOK, G. T. & STONE, Doris M.
Acute Respiratory Infections in Children. Isolation of Coxsackie B Virus and Adenovirus during a Survey in a General Practice. *Brit. Med. J.* 1960, Oct. 22, 1180-84, 1 chart. [17 refs.]

The authors studied a sample (about 20%) of those febrile respiratory illnesses for which a doctor was called and which occurred in the 595 children aged under 18 years of a practice on the south-west fringe of London. Cases of clinical influenza and specific fevers were excluded. Throat swabs were collected early in the illnesses and tested for pathogenic bacteria and also inoculated into HeLa cells. The authors point out that this technique would not have detected many known pathogenic respiratory viruses.

Coxsackie B3 virus was isolated from 18 cases, adenovirus types 1, 2, 3, and 4 from 1 case each, and *Streptococcus pyogenes* group A from 18 cases. Pneumococci were found in 25 cases but were not thought to be pathogenic. The isolations of Coxsackie viruses and streptococci were grouped together in epidemic form, the first in the summer of 1958 and the second in the early months of that year. An aetiological diagnosis had not in general been possible from clinical signs but retrospective analysis showed an increased frequency of myalgia in cases from which a Coxsackie virus was recovered, and an increased frequency of throat symptoms and signs, such as follicular exudate and enlarged tender upper cervical glands, in cases from which streptococci were recovered. The paper gives quite full clinical details, and includes 3 case-histories. [The main interest of this paper is the report of an epidemic of undifferentiated respiratory disease associated with Coxsackie B3 virus infection. JORDAN *et al.* also reported this in 1956 [see this *Bulletin*, 1957, v. 32, 731].]

D. A. J. Tyrrell

STALLONES, R. A., LENNETTE, E. H., NITZ, R. E. & HOLGUIN, A. H. **Evaluation of an Adenovirus Vaccine in a Dispensary Population.** *Amer. J. Hyg.* 1960, July, v. 72, No. 1, 100-110, 1 fig. [12 refs.]

From November 10 to 25, 1958, 1,762 military recruits (average age about 20 years) in 8 companies were vac-

inated at Fort Ord, California. 477 received 1 ml. of an aqueous polyvalent influenza vaccine; 401 received 1 ml. of an adenovirus vaccine containing types 3, 4 and 7; 421 received both vaccines, and 463 received 1 ml. of formol-saline. There was no reduction, attributable to the influenza vaccine, in the number of cases of respiratory illness needing medical attention, but only one person had serological evidence of influenza infection. However, the adenovirus vaccine caused a 58% reduction in respiratory illness. This effect seemed specific for there was no difference in the incidence of non-respiratory illness in the 4 groups. 12.5% of 104 paired sera from persons immunized against adenovirus infection showed a diagnostic rise in complement-fixing (CF) antibody and 54% of 294 paired sera from men not immunized were positive. The geometric mean CF antibody titre of the adenovirus-vaccinated group was about 4-fold lower than the unvaccinated group at the end of the 10-week period of observation. It was therefore considered that serological evidence of adenovirus infection in the vaccinated group would still be reliable.

On the basis of serological data, the adenovirus effectiveness was calculated to be about 90%. Throat washings from 75 patients with respiratory disease yielded an adenovirus on 18 occasions and these strains (all type 4 except for one type 7) came from persons who had not received adenovirus vaccine. Of 73 paired sera from these patients tested in CF tests, 51 were negative and an adenovirus was isolated from only 1, but 16 virus isolations were made from the 22 seropositive persons.

The allocation of companies of men, rather than individuals, to the vaccine groups required less record-keeping. Outbreaks of respiratory disease confined to each company and migration of individuals to and from companies might interfere with vaccine evaluation. These problems, and the comparability of results with the findings of previous studies, are discussed by the authors.

D. Taylor-Robinson

BEEM, M., WRIGHT, F. H., HAMRE, Dorothy, EGERER, Rosalie & OEHRME, Mafalda. **Association of the Chimpanzee Coryza Agent with Acute Respiratory Disease in Children.** *New England J. of Med.* 1960, Sept. 15, v. 263, No. 11, 523-30.

From December 1958 to June 1959, 291 patients were studied at the Bobs Roberts Hospital, Chicago, as follows: 83 in-patients with acute respiratory disease and 42 without respiratory disease; 85 out-patients with acute respiratory disease and 81 without respiratory disease. 48 cytopathic agents were isolated in stationary HEp-2 cultures at 36°C. from 27 in-patients and 14 out-patients with respiratory disease. The authors believe that the high rate of virus isolation was due to their practice of inoculating throat swab fluids without freezing them.

The prototype strain was termed Randall virus. On primary isolation a cytopathic effect was usually evident within 5 days and consisted of syncytial areas and giant cells. Growth in HeLa and KB cells was similar, but was slower in primary monkey kidney, human kidney and amnion. 80% of the isolations were from children below the age of 5 years who had been ill less than 1 week. The virus was antigenically similar to chimpanzee coryza

agent (CCA) since Long and Sue strains of CCA and Randall virus produced similar complement-fixing (CF) titres with paired sera of 5 patients from whom Randall virus was isolated; this was confirmed by cross-neutralization with specific immune rabbit antisera.

Bronchiolitis (17 cases) and bronchopneumonia (8 cases) were the most common forms of clinical illness. The croup syndrome was seen only once. The virus appeared to be responsible for the illnesses since it was (i) only isolated from patients with respiratory disease, (ii) demonstrated in the respiratory tract of 6 patients more than once, (iii) not demonstrated on convalescence and (iv) responsible for a 4-fold or more increase in CF antibody titre in 16 of 23 paired sera tested and in 14 produced a significant increase in neutralizing antibody.

D. Taylor-Robinson

DOSTAL, V., GÄDEKE, R., MITTELSTRASS, H. K., REIMOLD, G., SAUTHOFF, R., THOMSEN, R. & VIVELL, O. Symptomatik, Erregernachweis und serologische Untersuchungen bei Entero-Virusinfektionen im Kindesalter. Beobachtet am Krankengut des Jahres 1958 in der Universitäts-Kinderklinik Freiburg i. Br. [Clinical Features, Demonstration of Causative Organism and Serological Investigation of Entero-virus Infections in Children] *Deut. med. Woch.* 1960, July 15 & 22, v. 85, Nos. 29 & 30, 1301-6; 1331-7, 1358-60. [19 refs.]

The authors report the results of extensive virological and serological examinations carried out in 1958 on 275 children suffering from possible enterovirus infections in Freiburg im Breisgau, Germany. The results are presented in detail in a number of tables. 57 strains of virus were isolated from stools, throat washings or cerebrospinal fluid, including types 1, 2 and 3 poliomyelitis virus (26 strains), types 2, 5, 9 and 11 ECHO virus (10 strains), and types A2, A4, A9, B2 and B4 Coxsackie virus (11 strains); 10 strains were not identified. Mumps complement-fixing antibody was found in 24 of 55 patients (45%).

D. J. Bauer

PATTYN, S. R., DELVILLE, J. P. & PEEL, J., with the technical collaboration of A. GANTOIS. Étude des virus entériques dans la population congolaise infantile d'Elisabethville de 1957 à 1959. [Enteric Viruses in Congolese Children in Elisabethville from 1957 to 1959] *Ann. Soc. Belge de Méd. Trop.* 1960, Apr. 30, v. 40, No. 2, 389-407, 4 diagrams & 2 figs. on pl. [13 refs.]

This paper describes the isolation of enteroviruses from normal children under 7 years living in Elisabethville in the Congo. The study was conducted between June 1957 and February 1959. Stool specimens were inoculated on to HeLa and human amnion cell cultures and into suckling mice. By these methods about 50% of the children were found to be excreting a virus at any one time. Some strains of Coxsackie B were more easily isolated in tissue culture than in suckling mice; similarly, some Coxsackie A strains were isolated which either produced no lesions or only subclinical lesions in suckling

mice. It was found that the majority of adults tested had antibodies to ECHO viruses 6, 7, 8 and 9 and to one of the Coxsackie A strains (type 18) isolated. It is noted that in the Congo the incidence of enterovirus excretion was high at all times of the year and the importance of this for the effectiveness of living poliovaccine campaigns is stressed by the work of LEBRUN *et al.* [this *Bulletin*, 1960, v. 35, 794].

A. J. Beale

DONALDSON, S. N., DANE, D. S., BRIGGS, MOYA & NELSON, R. T. The 1957 Epidemic of Poliomyelitis in Belfast. *Ulster Med. J.* 1960, June 1, v. 29, No. 1, 14-21, 4 figs.

In 1957 there was a major outbreak of poliomyelitis in Belfast with 114 paralysed patients, an attack rate of 25 per 100,000. 81% of the patients were under 6 years old, none was under 6 months and only 4 were 7-12 months old. There were 2 deaths. 9 families had 2 or more reported cases of poliomyelitis but in only 2 families was there more than 1 paralytic case. The epidemic started early in the year but its maximum severity was in the summer months. Poliovaccination started in Belfast in May 1957 but supplies were limited and insufficient children were vaccinated to have any influence on the epidemic. Samples from 183 patients suspected of having poliomyelitis were examined for viruses; these cases included all those with paralysis. 159 patients were shown to be infected with poliovirus type 1. 2 out of 4 patients excreting an ECHO virus were paralysed. 20 patients could be serologically shown not to have been infected by poliovirus and 1 of these was paralysed. The incidence of poliovirus type 2 antibodies was much lower in paralysed patients infected with type 1 virus than in the general population of the same age (estimated from 1955 results, DANE *et al.* [this *Bulletin*, 1956, v. 31, 699]). This may mean that type 2 antibodies offer some protection against paralysis from type 1 infection.

112 paralysed children made good recoveries; 38 completely recovered and only 8 needed to attend a school for the physically handicapped. 4 of the paralysed patients had been inoculated with combined diphtheria-pertussis vaccine within 21 days and in 3 the onset of paralysis was in the inoculated limb. There was no evidence from the rate of smallpox vaccination in children under 3 to support the idea [*ibid.*, 498] that protection against poliomyelitis is conferred by vaccinia.

A. J. Beale

KALWIJ, A. S. De epidemiologie van de poliomyelitis in Nederland. [The Epidemiology of Poliomyelitis in Holland] [Thesis.] 138 pp., 5 charts. [Numerous refs.] English summary. 1959. Assen: Van Gorcum & Comp. N.V., Netherlands.

The author has carried out an epidemiological investigation of the incidence and distribution of poliomyelitis infection in 4 provinces of Holland between 1956 and 1958. During this time 266 cases of poliomyelitis were notified, 40% of which were studied by virological and serological methods. The investigations were also extended to 101 families in which a case of poliomyelitis

had occurred, to 20 unaffected families living in environmental contact with them, 3 children's residential institutions and a school. 63 strains of poliomyelitis virus were isolated from 74 patients, and 69 from 333 of their contacts in 71 families; type 1 predominated at the beginning of 1957, but gradual shift to type 3 was observed. The frequency of isolation of the virus from contacts was greatest in the 0-4 year age-group (37 of 53). There was no evidence of any seasonal variation in the distribution of virus in the infected environments. The virus could be isolated from the stools of healthy infected contacts for 4-6 weeks; among 316 persons investigated virus could be isolated from 77 (25%) during the first 3 weeks after exposure to infection, and from 41 of 410 during the second 3 weeks. No poliomyelitis virus could be isolated from 76 normal persons, including the members of 12 families in which no case of poliomyelitis had occurred, or from 1,336 stool samples collected from unspecified persons in 1958 in Amsterdam and Rotterdam. Poliomyelitis neutralizing antibody was found in a high proportion of the family contacts of patients suffering from the disease, and in the 0-9 year age-group only 3 of 84 had no antibody. *D. J. Bauer*

TODOROVICH, K., Poliomyelitis and Some Related Diseases in Yugoslavia. *Problems of Virology*. London. 1959, v. 4, No. 5, 34-9. [22 refs.] [Translated from Russian.]

The author feels that the epidemiology of poliomyelitis and related illnesses has not been sufficiently studied in Yugoslavia. Between 1952 and 1955, 18.73% of cytopathogenic viruses and in 1956 almost 40% could not be classified as poliovirus. An epidemic in Slovenia in 1956 was characterized by a large number of cases in which the patients had symptoms of meningitis but very little paralysis: the illness was later shown to be due to ECHO 9 virus. Thorough virological investigation of all outbreaks of poliomyelitis and related diseases is essential.

A. B. Christie

JUNGNER, I. & JUNGNER, G. Disturbances in Nitrogen Metabolism in the Acute Stage of Paralytic Poliomyelitis. *Acta Med. Scandinavica*. 1960, Nov. 1, v. 168, No. 3, 169-92, 12 figs. [60 refs.]

"The nitrogen excretion has been studied in about 30 cases of severe paralytic poliomyelitis, by analysis of a number of nitrogenous substances and fractions in the blood and urine. It is found that the great increase in nitrogen metabolism is expressed as a high output in the urine, as well as an increased blood content of substances which partake in nitrogen transport in the body, or are end-products of its metabolism.

"The possibility is discussed of calculating the remaining or functioning muscle mass on the basis of e.g. the total nitrogen, creatine and creatinine values in urine. It is pointed out that, in addition to the muscle destruction, unspecific inflammatory processes contribute to forming the chemical pattern of nitrogen metabolism in poliomyelitis."

VANNUGLI, R. La poliomielite in alcuni paesi Europei. La recente evoluzione epidemiologica ed i programmi di vaccinazione. [Poliomyelitis in some European Countries. The Recent Epidemiological Trend and Vaccination Programmes] *Ann. d. San. Pubblica*. Rome. 1960, July-Aug., v. 21, No. 4, 921-74, 9 graphs. [10 refs.] English summary.

GIBBELS, Ellen, SCHEID, W. & ACKERMANN, R., with the technical assistance of Brigitte HIERONYMI & Gisela STAUSBERG. Über die diaplazentare Übertragung neutralisierender Antikörper gegen die Poliomyelitisviren. [The Transplacental Transfer of Poliomyelitis Virus Neutralizing Antibodies] *Arch. f.d. gesamte Virusforschung*. 1960, v. 10, No. 2, 167-82, 3 figs. [27 refs.]

The authors have determined the content of neutralizing antibodies to the 3 types of poliomyelitis virus in the paired sera of 100 mothers aged 20-30 years and their newborn infants delivered in hospital in Cologne in 1957-59. In most cases the maternal antibodies were transmitted to the offspring; thus, 51 of 70 infants born to 70 mothers with all 3 types of antibody also possessed all 3 types, and a similar agreement was found in 19 of 21 infants born to 21 mothers with 2 types of antibody. The titres of the paired sera were in virtual agreement in 83 instances for type 1 antibody, and 85 and 67 instances for types 2 and 3 antibody respectively. Higher titres were found in the babies in only 9 instances, whereas the mothers had higher titres than their infants in 56 instances. The results indicate that types 1 and 2 antibody pass through the placenta easily and type 3 less readily.

D. J. Bauer

SALK, J. E. Persistence of Immunity after Administration of Formalin-Treated Poliovirus Vaccine. *Lancet*. 1960, Oct. 1, 715-23, 16 figs. [18 refs.]

This paper, based on an address at the 5th International Poliomyelitis Conference in Copenhagen in July 1960, is a spirited defence of killed poliovaccine as the method of choice for prophylaxis against poliomyelitis. It is shown that there was a straight line relationship between incidence of paralytic poliomyelitis and number of doses of poliovaccination in 1959 in the U.S.A. in children aged 0-4. In older people similar straight lines could be drawn although those unvaccinated had lower rates than would be predicted from the slope of the curve with increased dose. This Salk attributes to the fact that those who do not come forward for vaccination are less susceptible to poliomyelitis, as was observed in the original FRANCIS trial [see this *Bulletin*, 1955, v. 30, 663]. It is concluded that one dose protects a proportion of people and successive doses the same proportion. Figures from the U.S.A., Belgium, Mauritius and Sweden are compared for vaccine effectiveness, and Swedish vaccine is probably the best and U.S. the worst.

Although, from the above, it seems that one dose of really potent vaccine may be adequate for protection against paralysis, Salk reviews the evidence showing that the antibody titres are much higher if a vaccine is given

in divided doses and particularly if sufficient time is allowed to get a secondary type of response. Salk has shown that the level of booster response and persistence of antibodies thereafter depend upon the antigenic mass of the primary dose or doses. He believes that with a sufficiently potent primary stimulus the immunity so induced may be irreversible, *i.e.* lifelong either by way of persistence of antibody or by sensitization of immune mechanism. [Salk does not offer any new evidence for this view.] The killed vaccine of high potency required by Salk has been demonstrated to be possible of achievement by CHARNEY *et al.* [*ibid.*, 1958, v. 33, 411] but could also be achieved by using present vaccines with an oily or other adjuvant, and Salk seems slightly to prefer this approach.

[This paper is required reading for all concerned with polio vaccine programmes.]

A. J. Beale

AUERSWALD, W. & JÜRGENSSEN, O. Zur Frage der Antikörperbildung gegen Poliomyelitis bei Kleinkindern. Untersuchungen über die Wirkung eines Adjuvansimpfstoffes mit Antigenkomponenten gegen Kinderlähmung, Diphtherie, Pertussis und Tetanus. [**Poliomyelitis Antibody Formation in Young Infants. Investigations of the Effect of an Adjuvant Vaccine with Antigenic Components to Poliomyelitis, Diphtheria, Pertussis and Tetanus**] *Wien. med. Woch.* 1960, Aug. 6, v. 110, No. 31, 646-8, 1 fig. [11 refs.]

The authors have investigated the development of immunity to poliomyelitis in 36 infants aged 4-6 months who lacked neutralizing antibody in a titre of 4 or higher to at least one type of poliomyelitis virus. The vaccine contained the 3 types of virus and also diphtheria, pertussis and tetanus components adsorbed on aluminium hydroxide (1 mgm. per ml.) and was given subcutaneously in 3 doses of 1 ml. at intervals of 4 weeks. Blood was taken for antibody titration before vaccination, 1 week after the first dose and again after 1 and 3 months. In the first samples 25% of the children lacked antibody to type 1, 33% to type 2 and 72% to type 3, and the geometric mean titre for all types was 8. After 1 week geometric mean titres of 64, 64 and 128 to the respective 3 types were observed, and after 1 and 3 months (when 28 and 21 children were investigated) the mean titres were 64, 32 and 64. The results obtained were thus not in accordance with the generally held view that young infants give a poor immune response to poliomyelitis vaccination while under the influence of persisting maternal antibody.

D. J. Bauer

EELOCK, B. **Poliomyelitis Epidemic in Mauritius and the Effect of Vaccination.** *Brit. Med. J.* 1960, Oct. 29, 1272-6, 3 figs.

This is a description of an epidemic of poliomyelitis in Mauritius between June and September 1959. During the epidemic 97 patients with the paralytic disease were admitted to the Princess Margaret Orthopaedic Centre which serves the whole island and the patients came from all parts. The majority (87.6%) were under 5 years of age, but despite severe overcrowding there were no

multiple cases in families. In the much larger 1945 epidemic there were 24 multiple cases in families. The 1959 outbreak was the fourth major outbreak in Mauritius but was also the least severe. There were no deaths.

In September 1957 a large scale campaign of Salk vaccination had been started among the children aged 1 to 5 years. In the following year it was offered to all the children between 1 and 2 years and in April 1959 again to all the children between 1 and 2 years. An interval of 3 to 4 weeks was allowed between the first 2 doses and a third injection was given after an interval of about 7 months. By the end of June 1959, the time when the outbreak started, the vaccination campaign was nearing its end. Among the 125,118 children (aged 1-7) offered vaccine, there were 78 paralytic cases. There were 72 paralytic cases among the 25,790 children who were not vaccinated and only 1 among the 43,395 children who had received 3 injections of Salk vaccine. Thus, in the age-group 1 to 7 years the attack rate per 100,000 for the unvaccinated was 279.1 as compared with a rate of 2.3 among those who had received 3 doses of Salk vaccine. [Age specific attack rates are not given.]

Stools and serum samples from the first 9 patients were sent to Dr. J. H. S. GEAR of the Poliomyelitis Research Foundation Laboratories in Johannesburg and type 1 poliomyelitis virus was isolated from them all. On August 14th Dr. P. D. WINTER of these laboratories visited the island and since the epidemic was continuing it was decided to institute a vaccination campaign with the type 1 Sabin vaccine for children aged 6 months to 10 years. This vaccination programme was started on August 24, and in about 10 days 195,000 out of an estimated child population of 213,000 received the Sabin attenuated type 1 virus. After August 24, there were only 4 more cases. 3 had received the Sabin vaccine 11-13 days before the onset of their disease, and in 1 the onset occurred before administration of the Sabin vaccine. By the time the Sabin vaccine was administered it seems that the epidemic had started to decline. Samples of blood and stools were obtained from 510 and 202 children respectively before the onset of the vaccination campaign and arrangements were made to collect post-vaccination blood and stool specimens from the same individuals. It is hoped that these will give some idea as to whether the Sabin vaccine had any influence upon the course of the epidemic.

A. J. Beale

SABIN, A. B. **Oral, Live Poliovirus Vaccine for Elimination of Poliomyelitis.** [Editorial.] *Arch. Intern. Med.* 1960, July, v. 106, No. 1, 5-9, 1 fig.

In this editorial Sabin strongly advocates the use of oral attenuated vaccine embodying the strains selected by him. These, he contends, are more attenuated as judged by monkey neurovirulence than those developed by KOPROWSKI or Cox, but are equally immunogenic. [It is very doubtful if Dr. Koprowski would agree with this, see *Brit. Med. J.*, 1960, v. ii, 1013.]

Sabin first considers safety with particular attention to reversion to virulence. He admits that reversion to virulence for monkeys does occur, especially with type 3, but contends that there is no evidence that virulent

strains are selected in the intestinal tract of man. Safety is clearly established by Russian experience, especially in Estonia and Lithuania. Effectiveness has not been assessed in controlled trials because this is impossible with a vaccine that can be spread to the unvaccinated and where the possibility exists that the vaccine, by conferring intestinal immunity, may limit the community spread of polioviruses. [This intestinal immunity—like most immunity—is not absolute.] Two figures show that the number of cases of poliomyelitis in these 2 republics were much fewer in 1959 after the use of Sabin vaccine than in previous years. [Fuller details are given by CHUMAKOV *et al.* (see below).]

The problem of interference by other enteroviruses is mentioned but the method of overcoming this by mass feeding of all 3 types as used by SABIN *et al.* in Toluca [this *Bulletin*, 1960, v. 35, 1215] is thought to be satisfactory. Sabin concludes by drawing attention to the fact that there were nearly 6,000 cases of paralytic poliomyelitis in the U.S.A. in 1959, nearly 1,000 of whom had had 3 doses of Salk vaccine. He asks whether the medical profession in the United States is willing to take the steps necessary now to attempt to eliminate poliomyelitis with attenuated vaccine or to continue to pay the present price of ineffective control.

[Sabin believes that no improvement in Salk vaccine can overcome the apathy of those unwilling to be vaccinated. It seems, however, that the number of cases of poliomyelitis will decline when, and if, killed vaccine as potent as that described by HILLEMANN at the 5th International Poliomyelitis Conference in Copenhagen is universally used.]

A. J. Beale

RECHT, P. Où en est la vaccination antipoliomyélique par virus vivants atténués? [The Present Position of Anti-Poliomyelitis Vaccination with Attenuated Virus] *Bruxelles-Méd.* 1960, Oct. 9, v. 40, No. 40, 1363-84.

This is a very long review of the present position of attenuated poliovaccine based on the 3 recent conferences, in Moscow, in Washington and in Copenhagen. The author concludes that the vaccine is almost certainly safe, and that it is almost certainly effective in that antibodies are produced and a gastrointestinal immunity (partial) occurs. The best method of administration has still to be worked out but, in view of the possible genetic instability, mass campaigns are thought advisable at first. The selection of the best 3 strains from those available is thought to be difficult. [In both Russia and America the Sabin strains are preferred. The other strains are more neurovirulent for monkeys and in some areas where they have been used cases of poliomyelitis have occurred which may have been due to them.]

A. J. Beale

CHUMAKOV, M. P., *et al.* Preliminary Report on Mass Oral Immunization of the Population against Poliomyelitis with Live Virus Vaccine from Attenuated Strains of Sabin Vaccine. *Problems of Virology*. London. 1959, v. 4, No. 5, 6-20. [Translated from Russian.]

The authors first give brief reasons for thinking that living attenuated poliovaccine is the most promising

method for mass campaigns against poliomyelitis. They describe a study of the effectiveness of mass oral immunization against poliomyelitis since "the question of the safety of the Sabin strains to be used was taken for granted". As a result of their studies involving the administration of vaccine to many people without antibodies in Lithuania and Estonia (304,521 type 1, 136,025 type 2 and 353,402 type 3) this conclusion is reinforced. [The details of the organization and surveillance are not given.] In all, in Estonia, Lithuania, and Kazakhstan by the 10th June 1959, 2.25 million had type 1 vaccine, 1.5 million type 2 and 1 million type 3. Approximately 50% of individuals in the most susceptible age-groups were vaccinated against type 1. Some serological results of immunization are shown. 77 out of 117 individuals without type 1 antibodies developed them as a result of vaccination, while at the same time, as a result of natural infection, 49 out of 85 individuals without type 2 antibodies developed them (there was a type 2 case of poliomyelitis in the children's home where the study was carried on 4 days before living type 1 vaccine was given) and 11 out of 123 individuals without type 3 antibodies developed them.

The geometric mean titres of a small group of children without antibodies after a dose of trivalent vaccine were type 1 1/45, type 2 1/208, type 3 1/97, with the colour test method of titration. The results of using a trivalent vaccine were little, if at all, inferior to the successive administration of monovalent vaccine, although the authors think it too early to be sure on this point and believe 2 doses of trivalent vaccine (10^5 TCD₅₀ of each type) may be necessary. The co-existence of wild type 2 virus and the vaccine strains in a children's home did not upset the establishment of successful vaccination. This good result is probably partly explained by the ease with which virus spread to contacts. Thus in a small group, 100% of contacts under 3 years became infected. Adults were much more rarely infected—31% of those not given Salk vaccine and 8% who had had a dose of this vaccine. Similarly, it was found that the duration of virus excretion was greater in children than in adults. Preliminary results from Lithuania and Estonia suggest that the incidence of poliomyelitis is much lower than in previous years, without the usual seasonal peak. In March to August, 1959, in Estonia there were 16 cases, 6 of whom had been vaccinated. Between May and August in Lithuania there were 17 cases, 4 of whom had been vaccinated. In the previous year in the same period there were 194 cases in Estonia and 129 cases in Lithuania. The authors hope that in a short while living vaccine will eliminate the threat of poliomyelitis epidemics.

A. J. Beale

GEORGIADIS, J. Research on the Penetration of the Attenuated Polio Virus Strains Type I (Chat) into an Unvaccinated Population in Wyszaków and the Surrounding District. *Bull. Inst. Marine Med Gdańsk*. 1960, v. 11, Nos. 1/2, 75-84, 5 graphs.

This study was carried out in contacts of vaccinated persons in the autumn and winter of 1958. Very few virus isolations were made even though sanitary conditions were bad, and it is concluded that this virus does

not spread in the community. No studies of the isolation of virus from vaccinated persons are presented.

A. J. Beale

HEGGIE, A. D., SCHULTZ, I., GUTEKUNST, R. R., ROSENBAUM, M. & MILLER, L. F. **An Outbreak of a Summer Febrile Disease caused by Cocksackie B-2 Virus.** *Amer. J. Pub. Health.* 1960, Sept., v. 50, No. 9, 1342-8, 2 figs. [13 refs.]

In the summer of 1958 there was a widespread occurrence of febrile disease among service families at the Great Lakes Naval Training Centre. The main features of the illness were fever and sore throat. Headache and diarrhoea occurred in slightly fewer patients and chest pain was experienced by about one-fifth of them. A sample of this population was studied involving 1,559 subjects in 392 families. 31% of these subjects were ill, 42% of those under 12 and 21% of those over 12. Cocksackie B2 virus was isolated from throat swabs or rectal swabs from 35 out of 361 people tested. During the 40-day period of the study virus was isolated from 15% of the subjects who had symptoms and from 3% of those who did not have symptoms. The low isolation rate is almost certainly explained by the fact that only 1 attempt was made and this was not always optimally related to the onset of symptoms. The virus was more frequently isolated in monkey kidney than in HeLa cell cultures. Thus, 21 specimens were positive in monkey kidney but negative in HeLa cells, whereas 7 were positive in HeLa but negative in monkey kidney cells. In addition to the 35 Cocksackie B2 strains 10 other virus strains were isolated as follows: adenovirus type 1, 2; ECHO viruses, 3; poliomyelitis viruses, 4; Cocksackie B3 virus, 1. No cases of aseptic meningitis were seen during this outbreak.

A. J. Beale

FELICI, A., ARCHETTI, I., RUSSI, F., BELLOCCHI, C. & MAZZI, F. Contributo allo studio delle malattie da virus Cocksackie. Manifestazione epidemica ad impropria diarroica causata da un virus Cocksackie tipo B3. [A Contribution to the Study of Cocksackie Virus Diseases. An Epidemic of Diarrhoea caused by Cocksackie Virus Type B3.] *Riv. Istituto Sieroterap. Ital.* 1960, May-June, v. 35, No. 3, 377-89, 7 figs. English summary (8 lines).

This is a report of the epidemiological, clinical and microbiological findings in an epidemic of 70 cases in a village with a population of 1,715 near Ancona, occurring between June and October 1959. 41% of the patients were under 10, 25.7% between 10 and 20, and 15.7% between 20 and 30. The illness was characterized by a sharp rise of temperature, headache and, in 54% of cases, by passage of liquid motions. In children under 11 there was a short lasting maculo-papular eruption. Some patients showed splenic and hepatic enlargement. There was vomiting in 25% as well as diffuse pains in the same proportion.

Throat washings from 22 patients yielded 5 isolations of B3 Cocksackie virus and 34 samples of faeces gave 11 positive results, while 34 samples of faeces from healthy

contacts gave 4 positives. Serum neutralization tests in 42 cases gave positive results in most, but 20%, including one patient from whose faeces the virus had been isolated, showed no antibodies. The 8 healthy contacts examined serologically gave positive results.

The authors believe the microbiological findings and the epidemiology justify the view that Cocksackie B3 virus was the aetiological agent.

E. Agius

WALTERS, J. H. **Postencephalitic Parkinson Syndrome after Meningoencephalitis due to Cocksackie Virus Group B, Type 2.** *New England J. of Med.* 1960, Oct. 13, v. 263, No. 15, 744-7. [41 refs.]

A woman aged 54 developed meningoencephalitis, the convalescent stage of which blended with the onset and development of a severe Parkinsonian state. Cocksackie virus group B, type 2 was isolated from the faeces and the neutralization titre of the serum was 1 in 256 at the onset of the illness and 1 in 512 one month afterwards. The incidence of Parkinsonism after illness other than encephalitis lethargica is reviewed.

A. B. Christie

TAKOS, M. J., WEIL, M. & SIGEL, M. M., with the technical assistance of G. G. SCHLAEPFER, M. C. LAUNER & R. V. CATING. **Outbreak of ECHO 9 Exanthema traced to a Children's Party.** *Amer. J. Dis. Children.* 1960, Sept., v. 100, No. 3, 360-64, 1 fig.

A small outbreak of 18 cases of ECHO 9 disease (usually manifested clinically in outbreaks in which at least a proportion of the patients have serious meningitis and a rash) occurred as a result of a children's party, although a few of the cases may have been familial infections. The illness was highly infectious, with an incubation period of 3-8 days. There was fever in all 12 of the children affected, and a rash on the buttocks (an unusual site) in 11 out of 12 children and 2 out of 6 adults. Although headaches were recorded there was no evidence of meningitis in this outbreak. ECHO 9 virus was isolated from the stools and throat washings of some of the patients, and, like the Cocksackie group and some of the epidemic strains of the ECHO group of enteroviruses, it was pathogenic for infant mice.

H. Stanley Banks

FAULKNER, Ruth S. & OZERE, R. L. **Aseptic Meningitis due to Type 19 Echo Virus Infection.** *New England J. of Med.* 1960, Sept. 15, v. 263, No. 11, 551-2.

A case of abacterial meningitis in a man of 49 is described. ECHO 19 was isolated from the cerebrospinal fluid. It seems probable that this man was infected by his daughter or her infant who visited him 2 days after recovering from an illness associated with anorexia, vomiting and diarrhoea. The man's wife, his other daughter and her husband suffered from a mild illness at the same time as he did characterized by fever, malaise, headache and nausea. 8 months later these 4 persons had

neutralizing antibodies to ECHO 19 virus whereas 2 laboratory workers did not. The virus was isolated in human amnion cells but could be readily adapted to monkey kidney cells. LAHELLE [this *Bulletin*, 1960, v. 35, 94] has described haemagglutination by ECHO 19 prototype strain, but this new strain did not agglutinate red cells. It also appeared to grow to higher titres and be less sensitive to inactivation at 37°C. than the prototype strain [this *Bulletin*, 1959, v. 34, 837]. ECHO 19 was originally isolated by RAMOS-ALVAREZ and SABIN [*ibid.*, 1958, v. 33, 1115] from children with diarrhoea, but this is the first time it has been isolated from a patient with abacterial meningitis.

A. J. Beale

DAVIES, D. M. Epidemic Cervical Myalgia. *Lancet*. 1960, June 11, 1275-7.

Two epidemics of stiff neck in 13 student nurses at the London Hospital are described, the first in the autumn of 1958 and the second one year later. The main feature was severe stiff neck with localized tenderness of trapezius. There was fever in 6 cases. The sedimentation rate and blood picture were normal. No evidence of virus infection was obtained, but in diagnostic despair the author feels that a virus might well have been responsible. Serological tests were performed for influenza (A, B, C), parainfluenza 1, mumps, adenovirus, psittacosis and Coxsackie B 1-5. Stool specimens were inoculated into suckling mice and HeLa cells. The author discusses the clinical points of difference between his patients and those with Bornholm disease, concluding that the two conditions are quite distinct.

A. J. Beale

KÜHN, H. A. & BAUR, H. Vergleichende Therapie der akuten Virushepatitis. [A Comparison of Various Forms of Treatment of Acute Viral Hepatitis] *Deut. med. Woch.* 1960, Nov. 4, v. 85, No. 45, 1956-65, 2005-6, 6 figs. [50 refs.]

In the years 1956-59, 10 German clinics collaborated in an investigation to compare the efficacy of various forms of treatment of acute viral hepatitis. This paper contains a careful and detailed account of the investigation and its results. 404 patients were chosen according to certain criteria, which are stated, in order to set up comparable groups. These patients were placed in the treatment groups (1) a described basic therapy only, and in the remainder basic therapy plus (2) intravenous Hep-san (acetyl-methionine-choline and sodium acetyl methionine), (3) prednisone, (4) BAL, (5) vitamin B12 and (6) thioctic acid. There is description and many tables of the findings in regard to length of stay in hospital, bilirubin levels, duration of jaundice and complications.

The main conclusion was that these treatments did not differ from one another when judged by duration of illness or length of stay in hospital. Prednisone did cause an earlier fall in serum-bilirubin concentration but did not influence the length of stay in hospital, nevertheless it is recommended on clinical grounds to be used in severe cases and those in which improvement is delayed.

The problem of treatment of viral hepatitis is not resolved and action must lie in prophylaxis by hygienic

methods and injection of gamma globulin. Active immunization may become possible when the causative organism can be isolated and cultured.

M. E. Delafield

VARMA, M. G. R. Preliminary Studies on the Infection of Culicine Mosquitoes with the Tamilnad Strain of West Nile Virus. *Indian J. Med. Res.* 1960, Sept., v. 48, No. 5, 537-48. [15 refs.]

The G2266 (Tamilnad) strain of West Nile virus isolated from *Culex vishnui* near Vellore was used after 3 mouse passages. The mosquitoes used were Indian strains. 30 *Culex pipiens fatigans* and 36 *Aedes albopictus* were inoculated thoracically with about $10^{4.1}$ LD50. After 1 day the titres were 4.8 and 4.5 log respectively and by the 7th day equal to or greater than ($\geq$) 6.7 and $\geq$ 7.6 log respectively. Virus remained detectable for at least 35 days in *C. pipiens fatigans* and at least 21 days in *A. albopictus*. 10 mosquito-mosquito passages were made in each species and the final titres were $\geq$ 6.2 and 5.0 log respectively. Inoculated *C. pipiens fatigans* transmitted by bite to suckling mice and chicks after 13-34 days' incubation. Positive transmissions were also achieved with *A. albopictus* after 9-13 days' incubation.

Chicks were found to have viraemia titres of $\geq$ 5.0 log 2-3 days after infective mosquito bite. The highest blood titres in 10-day-old mice thus infected were 3.0 log on the 2nd day, and $\geq$ 2.7 log on the 3rd day.

Mosquitoes were infected by feeding on these hosts and *C. pipiens fatigans* was found to have a titre of 4.5 log 40 days after feeding. The peak titre ($\geq$ 6.2 log) was after 20 days' incubation. *A. albopictus* titred $\geq$ 5.5 and 4.5 log after 50 days' incubation. Transmission to chicks was effected by bite of *C. pipiens fatigans* 17-62 days after an infective feed and by *A. albopictus* 10-42 days after. Virus was recovered from *C. pipiens fatigans* 62 days after the infective meal and from *A. albopictus* after 57 days. 3 chick-mosquito cycles were made successfully with *C. pipiens fatigans* and 2 with *A. albopictus*. *C. vishnui* were inoculated with a large dose of virus: from a titre of 4.7 log immediately after inoculation titres of $\geq$ 7.3 log on the 4th and 5th days and of 7.5 log on the 10th day after inoculation were reached. Transmission to chicks and suckling mice by bite was successful after 3-20 days' incubation with inoculated *C. vishnui*.

C. E. Gordon Smith

ANDERSON, S. G., PRICE, A. V. G., NANADAI-KOIA & SLATER, K., with the technical assistance of Margaret McELROY. Murray Valley Encephalitis in Papua and New Guinea: II. Serological Survey. 1956-1957. *Med. J. Australia*. 1960, Sept. 10, v. 2, No. 11, 410-13, 2 figs.

Sera were collected in the second half of 1956 from several areas of eastern New Guinea and from New Britain. Persons aged under 15 were called children. The sera were tested after heat inactivation for neutralizing antibody to Murray Valley and Japanese encephalitis viruses by an intraperitoneal test in suckling mice. Undiluted unheated rabbit serum was added. No antibody

to Murray Valley virus was found in the Central Highlands (48 children, 29 adults, 94 chickens), Rabaul (25 human beings, 22 chickens) or in 5 coastal areas of New Guinea (63 children, 93 adults, 73 chickens). However, 4 of 39 adults from Kaiapit (Markham Valley) had Murray Valley antibody, as did 2 of 53 children aged 2-4 years, 6 of 95 aged 5-9 years and 21 of 121 chickens from the Sepik River, 5 of 6 children aged 2-4, 36 of 45 aged 5-9, all of 7 aged 10-14 and 12 of 60 chickens from the Aramia River, 6 of 57 children aged 2-4, 10 of 57 aged 5-9, 10 of 54 aged 10-14, 54 of 72 adults and 26 of 145 chickens from the swamps behind Port Moresby. 31 wild birds of 6 species were shot, mostly on the Aramia River and 19 had Murray Valley antibody.

Representative positive sera were titrated in a serum dilution test against both viruses. The average titre against Murray Valley was higher in human than chicken sera. In the Sepik River area and in the Port Moresby swamps the titre against Murray Valley was never less than against Japanese encephalitis; and on the Sepik River none of 34 sera without Murray Valley antibody had antibody to Japanese encephalitis. On the Aramia River, of 16 sera titrated 8 had higher titres against Japanese encephalitis and 4 had similar titres against both viruses. This may indicate a heavier infection rate in this area or the presence of related viruses other than Murray Valley. [See also this *Bulletin*, 1958, v. 33, 536.]

C. E. Gordon Smith

LAMOTTE, L. C., Jr. **Japanese B Encephalitis Virus in the Organs of Infected Mosquitoes.** *Amer. J. Hyg.* 1960, July, v. 72, No 1, 73-87, 4 figs. [11 refs.]

The T-485 strain of Japanese encephalitis virus isolated from *Culex tritaeniorhynchus* in the third mouse-brain passage was used. Mosquitoes were maintained at $80 \pm 2^\circ\text{F}$. Chicks 4-12 hours old infected intradermally had viraemia (10^3 - $10^{5.5}$ LD₅₀/0.03 ml.) 48-72 hours later. 20 days after feeding on such chicks 91-100% of 4 *Culex* species (*quinquefasciatus* [*pipiens fatigans*], *p. pipiens*, *p. var. molestus*, *tarsalis*) were infected and 82-100% transmitted to chicks by bite: of *Aedes triseriatus* 100% were infected and 52% transmitted, of *A. aegypti* 22% and 19%, of *Psorophora confinnis* 74% and 7%; no *A. albopictus* were infected. When *C. quinquefasciatus* were fed on blood with 1.4-3.5 log LD₅₀/0.003 ml. the infection rate after 17-19 days was 23% at 1.4 log, and 88% or more at 1.8 log or more: transmission rates were 13% at 1.4 log, 37% at 1.8 log, 68% at 2.5 log, 89% and 81% at 2.8 and 3.5 log. Mosquitoes containing over 4 log LD₅₀ 10 days after feeding were able to transmit while those with lower titres did not.

The virus contents of head, thorax and abdomen of *C. pipiens* were determined at intervals after infection: in the first week virus was usually detected only in the abdomen but by the second or third week all parts of the mosquito were infected. During the 4th and 5th weeks there tended to be more virus in thorax than abdomen. More extensive dissection of *C. pipiens* 48 days after infection revealed high titres in head, prothoracic, salivary glands and thoracic nerve ganglia; little or no virus was found in the gut or diverticula, thoracic

muscle or fat body, haemolymph, Malpighian tubules, ovaries, abdominal ventral nerve. The abdominal part of the mid-gut was the only tissue in which virus could be detected during the 1st week and during the 2nd week the titre was 2-4 log LD₅₀. After this the mid-gut titre fell rapidly. Virus was found in the haemolymph in the 2nd to 4th weeks and thus in the organs. Titres of 4-5 log LD₅₀ were reached in the salivary glands by the end of the 2nd week and maintained at least till the 7th week. High titres were also maintained in cephalic and thoracic nerve ganglia.

Infected *C. pipiens* survived as long as uninfected and no histological change could be found in infected mosquitoes.

C. E. Gordon Smith.

YAV'IA, A. R. **Seroprophylaxis of Tick-Borne Encephalitis.** *Problems of Virology*. London. 1959, v. 4, No. 6, 50-54. [Translated from Russian.]

Between 1954 and 1958, 3,541 persons consulted hospitals in Tomsk after tick bites and of these 1,816 were injected with crude encephalitic antiserum: 1.8% of the inoculated persons developed tick-borne encephalitis compared with 6% in the uninoculated. In 1958, 397 persons were injected with purified encephalitic antiserum and 338 with anti-encephalitic gamma globulin: in each group, tick-borne encephalitis occurred in 1.5% compared with 6% which would be expected in the uninoculated according to the 1954-56 figures: there were no other controls. Serum sickness occurred 2-4 times less frequently with the purified anti-serum or gamma globulin.

A. B. Christie

KARPOV, S. P. **Prophylaxis of Tick-Borne Encephalitis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 11, 4-9. [11 refs.] [Translated from Russian.]

The most efficient prophylactic measure for the prevention of tick-borne encephalitis is the wholesale destruction of ticks on the domestic animals in the area. Spraying with 10% DDT dust was found to be superior to BHC and systematic use of this measure over a period of 3 years led to the complete elimination of ticks from the area. The use of a virus vaccine much reduced the incidence of the disease in man and for individual protection of those bitten by ticks anti-encephalitis gamma globulin was found to be effective. Even in cases where the vaccine or the gamma globulin failed to prevent infection the clinical course of the disease was much milder than in those who had not received these measures.

H. J. Bensted

KOKERNOT, R. H., SMITHBURN, K. C., PATERSON, H. E. & DE MEILLON, B. **Further Isolations of Wesselsbron Virus from Mosquitoes.** *South African Med. J.* 1960, Oct. 8, v. 34, No 41, 871-4. [17 refs.]

12 strains of virus were isolated by inoculation of suckling mice with pools of 44-218 *Aedes* (*Ochlerotatus*) *caballus* collected near Middelburg in Cape Province.

3 strains were isolated similarly from pools of 4-48 *Aedes* (*Neomelaniconion*) spp. from the same area. 1 strain was isolated from a pool of 41 *Mansonia* (*Mansonioides*) *uniformis* and 1 from a pool of 106 *Culex* (*Culex*) *univittatus* from Ndumu in Natal. The strains were not fully pathogenic for adult mice inoculated intracerebrally until after 2 infant-mouse passages. A combination of haemagglutinin-inhibition, complement-fixation and neutralization tests was used to demonstrate that all 18 strains were closely related to or identical with Wesselsbron virus.

The incidence of virus infection in mosquitoes near Middelburg at the time of these isolations (1957) was so high that either Middelburg or Wesselsbron virus was isolated from 29 of 30 pools of *A. caballus* and from 4 of 4 pools of *Neomelaniconion* spp. Some of the isolates were subsequently shown to be mixtures of these 2 viruses.

[See also this *Bulletin*, 1958, v. 33, 717, 1001.]

C. E. Gordon Smith

BLACK, F. L. & YANNET, H. **Inapparent Measles after Gamma Globulin Administration.** *J. Amer. Med. Ass.* 1960, July 16, v. 173, No. 11, 1183-8, 1 fig. [18 refs.]

During the course of measles epidemics in an institution for mentally retarded children, 19 out of the 38 susceptible children who were exposed to the infection and were given gamma globulin developed measles antibodies without overt signs of measles. When sera were tested 7 weeks after the infection, those children who had no apparent infection showed generally a lower titre than those with overt disease. 5 of the 19 who developed antibodies failed to contract measles when again exposed to the infection 7 months later. In order to avoid the needless administration of gamma globulin in subsequent exposure, it is suggested that the complement-fixation test might be used to determine the immune status of children exposed to measles who remain asymptomatic after receiving a dose of gamma globulin.

D. A. Cannon

DOLGIN, J., LEVINE, S., MARKHAM, F. S., CABASSO, V., WEICHSEL, M., RUEGSEGER, J. M. & COX, H. R. **Immunizing Properties of Live Attenuated Measles Virus.** *J. Pediatrics.* St. Louis. 1960, July, v. 57, No. 1, 36-41. [10 refs.]

The immunizing properties of 2 types of live attenuated measles vaccine prepared from the Edmonston strain were investigated in 2 groups of children. The first group were injected subcutaneously with 0.5 or 1 ml. of vaccine prepared from virus passaged in the amnion and containing 3,000 and 6,000 TCD₅₀ respectively. 6 children had no neutralizing antibody before vaccination, but developed titres of 89-354 by the 25th day; they all developed a febrile illness lasting for 2-4 days after the incubation period of 5-8 days, with a faint transient maculopapular exanthem in the 4 instances, but without Koplik spots or the catarrhal manifestations of natural measles. The remaining 4 already had antibody before

vaccination. The second group received vaccine prepared from virus grown in cultures of chick embryo tissues in doses of 50 or 100 TCD₅₀; 5 who lacked antibody before vaccination developed titres of 16-89, but none developed any signs of modified measles infection. In a further group of 10 susceptible children given amniotic vaccine in doses ranging from 6 to 6,000 TCD₅₀ an antibody response occurred in all instances, and 8 children developed an illness resembling a mild attack of measles, including the 3 who had had the lowest dose of vaccine.

D. J. Bauer

STOKES, J., JR., REILLY, C. M., HILLEMANN, M. R., & BUYNACK, E. B. **Use of Living Attenuated Measles-Virus Vaccine in Early Infancy.** *New England J. of Med.* 1960, Aug. 4, v. 263, No. 5, 230-33. [11 refs.]

The authors have investigated the effect of live attenuated measles vaccine in 13 infants born in an institution who had not been exposed to measles. The vaccine was injected subcutaneously in a dose of 0.25 cc. and observations were carried out for 1 month. The 5 oldest infants (7-13½ months) had no antibody before vaccination, and all apparently developed an infection with measles virus, with pyrexia of 2-5 days' duration, a rash in 2 instances, and the appearance of neutralizing and complement-fixing antibodies to titres of 16-128 and 20-80 respectively. The illness was mild in 4 instances. The 8 youngest infants (4-6 months) had antibody before vaccination; only 1 developed a febrile illness, and none showed any significant rise in antibody titres, and infection with the vaccine virus was evidently suppressed by the pre-existing immunity. A susceptible unvaccinated infant who was left in contact with the others showed no evidence of infection.

D. J. Bauer

MICHAELS, R. H. & MELLIN, G. W. **Prospective Experience with Maternal Rubella and the Associated Congenital Malformations.** *Pediatrics.* Springfield, Ill. 1960, Aug, v. 26, No. 2, 200-209. [35 refs.]

"The Fetal Life Study" began in 1946 to study factors relating to, among other things, abortion and congenital malformations. Between that date and 1959 examination was made of the results of 25 instances of rubella during pregnancy. In the majority of cases the diagnosis of rubella was made at the time of its occurrence by a physician; in the remainder by a careful study of the history. But it is pointed out that because no specific laboratory confirmation is yet available the diagnosis of this disease must rest on clinical observation. The study is based on the experience of all pregnant women registered in the ante-partum clinic of the Sloan Hospital within the first 14 weeks following the onset of their last menstrual period—some 10,000 women within the 13 years of this survey.

In the first 4 weeks of pregnancy 2 cases of rubella were reported. One infection occurred during the last menstrual period and a normal infant was later delivered

The other infection, in the 3rd week of gestation, was followed by spontaneous abortion. The 7 pregnancies complicated by rubella in the 5th–8th weeks resulted in 3 spontaneous abortions, 3 malformed live infants and 1 normal infant. Rubella infection after the 8th week in 16 instances revealed no abnormalities in the progeny

in a follow-up period which in no case extended beyond 2½ years.

It is concluded that prospective observations on this subject should be more completely reported and that there is need for objective laboratory techniques for the diagnosis of rubella.

J. Pickford Marsden

Bacteriology and Immunity

The order in this section is:—General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. Their titles and page references are cited below in the appropriate sub-divisions of this section.

GENERAL

BRITISH COMMONWEALTH. Collections of Micro-Organisms. Directory of Collections and List of Species maintained in [a] Australia, pp. v + 45. [8s.] [b] Canada, pp. iv + 48. [9s.] [c] India, pp. iv + 36. [6s.] [d] New Zealand, pp. iv + 16. [3s.] [e] United Kingdom, Ghana and Trinidad, pp. iv + 70. [12s. 6d.] London: H.M. Stationery Office.

The new edition of each of these 5 Directories has been published on the decision of the Permanent Committee of the British Commonwealth Specialist Conference on Culture Collections. The Directories are clearly produced and are similar in form except for minor variations. Each of these contains: (i) a list of the collections and each of their code numbers, the names of the scientific personnel and some particulars of distribution of cultures; there is a separate numerical list of the collections; and (ii) a list of species maintained in the collections under such headings as those for the United Kingdom, *viz.*: algae and protozoa, bacteria, bacteria grouped according to their biological activity, fungi, viruses and bacteriophages, and yeasts. There are certain differences in these headings, as for example in the Australian Directory which separates animal, insect and plant viruses and also includes protozoa, metazoa and animal tissue cultures. The sources of the adopted nomenclature of the species are also sometimes stated.

M. E. Delafield

SERFONTEIN, W. J. & WEYLAND, H. A Laboratory Scale Apparatus for the Continuous Culture of Micro-Organisms with Automatic pH Control. Onderstepoort J. Vet. Res. 1959, July, v. 28, No. 1, 39–45, 4 figs. [10 refs.]

A relatively simple adaptation of the chemostat of MONOD [this *Bulletin*, 1951, v. 26, 1101] is described. Control of flow of culture fluid and the addition of acid

or alkali is by the application of suction. Gas is bubbled through only a small part of the medium, and not the main bulk of nutrient, thus reducing the risk of decomposition of the nutrients. The pH is measured by the usual glass/calomel electrode system and the potential registered determines, after amplification, the level of the gas pressure over the acid and alkali tanks and therefore the amount of each fed into the culture. It is claimed that this apparatus, which can be made in any laboratory with elementary glassblowing facilities, lowers the risk of contamination in long-term experiments. [Only the barest description is given of the automatic control system although a reference is made to technical advice given by a commercial firm.] *R. B. Morrison*

ADAMOV, A. K. Selective Adsorption as a Method for the Rapid Removal of Saprophytic Organisms from Mixed Suspensions with Pathogenic Organisms. J. Microbiol., Epidemiol. & Immunobiol. London. 1959, v. 30 No. 12, 5–10. [10 refs.] [Translated from Russian.]

Certain chemical compounds appear to have affinities for certain types of bacteria, which vary according to the bacterial types. Substances like charcoal seem to be able, however, to adsorb most bacteria to a very high capacity. The author examined a great many substances for their selective adsorptive capacity and found one, tricalcium phosphate, that selectively adsorbed Gram-positive cocci and Gram-negative saprophytic organisms without seriously affecting the typhoid and paratyphoid organisms that were in the mixture. This is true only of smooth organisms, for R forms of both *Salmonella typhi* and *Salm. paratyphi* are adsorbed by tricalcium phosphate 7–8 times more readily than S forms of these organisms.

[It would seem that the method has been examined only with artificially mixed cultures; whether it would be

effective in natural mixtures such as faeces is not known, but it is an interesting observation and may have useful applications.]

H. J. Bensted

VERENINOVA, N. K., SMIRNOVA, E. J., KALACHEVA, N. F., KUZNETSOVA, N. J., MELNIKOVA, A. F. & DOBROTS-VETOVA, T. Y. **The Efficacy of Combined Vaccination with Live Vaccines against Plague, Tularaemia, Brucellosis and Anthrax. II. Degree of Immunity to Intratracheal Infection following Combined Vaccination of Guinea-Pigs.** *J. Microbiol., Epidemiol. & Immunobiol.* London, 1959, v. 30, No. 11, 18-24. [Translated from Russian.]

In a previous communication [this *Bulletin*, 1959, v. 34, 1109] the authors showed that while a combined vaccine against plague, tularaemia and brucellosis gave adequate protection in guineapigs when subsequently challenged with virulent organisms, a combined vaccine which also contained the anthrax antigen was not effective against anthrax although it had about the same efficacy against plague, tularaemia and brucellosis as the

previous vaccine. If the anthrax vaccine were given separately some 10 days before the triple vaccine the guineapigs were protected adequately against all four infections when challenged subcutaneously. The present paper records a repetition of the previous experiments but with the challenges administered by the intratracheal route. The results were very similar to those recorded in the previous paper, but the anthrax vaccine was poor even when given 10 days before the triple vaccine. Incidentally, the authors found that the percutaneous method of vaccination was very suitable for the living plague vaccine.

H. J. Bensted

BULLOCH, W. **The History of Bacteriology.** Heath Clark lectures, 1936.

This book was reviewed on p. 101.

BISSET, K. A. & DAVIS, G. H. G. **The Microbial Flora of the Mouth.**

This book was reviewed on p. 102.

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—General; Antibiotics; Colicines; other Therapeutic Substances; Disinfection.

J. MED. LAB. TECHNOL. 1960, July, v. 17, No. 3, 133-43.

A Survey of Antibiotic Sensitivity Tests. Bacteriological Section of the Advisory Committee on Medical Laboratory Techniques [TILL, D. H. (Chairman), BARSON, G. F., BEVIS, M. A. & HURST, L.]

This is a report of an enquiry undertaken by the Birmingham branch of the Institute of Medical Laboratory Technology. A questionnaire about methods used for determining bacterial sensitivity to antibiotics was sent to laboratories in the Midlands: of 48 replying, 26 used a proprietary tablet, 12 filter paper discs, and the rest a variety of methods or combinations thereof. A further questionnaire and 6 cultures for test were then sent out, and results were received from 33 laboratories. These cultures were a streptococcus (not further identified) and 5 staphylococci, 1 of which was the standard "Oxford" strain. The only antibiotic with which tests were done in all laboratories was penicillin, but a majority used 4 others, and fewer laboratories used some of a variety of 16 other substances, including 3 synthetic compounds.

The results, which are given in full and in several analysed forms, show frequent and extensive discrepancies, particularly in tests with penicillin, streptomycin and novobiocin, and with 2 of the organisms, one being the streptococcus (*e.g.*, in tests of this organism with penicillin, there were 8 reports of sensitivity, 19 of resistance and 6 doubtful: the corresponding figures for

culture 5, a staphylococcus, are 11, 19 and 3). A few laboratories even reported the Oxford staphylococcus resistant to penicillin and to each of the 3 tetracyclines.

There is a discussion of possible factors which might account for these differing results: information provided about the quantities of antibiotics used in the tests, the diameter of inhibition zones observed, the size of the inoculum (when specified) and culture media used does not point to any single factor as responsible. The authors evidently find these results disquieting, and suggest that known sensitive and resistant strains of organisms should be included in all tests, and that zones of inhibition should be accurately measured. [This report would have been of much more value if the authors had given the correct answers. They do not even identify the streptococcus: was it a strain of *Streptococcus faecalis*? If all or most of the errors were in calling sensitive organisms resistant, defective discs or tablets—whether badly prepared, damaged by moisture or time-expired—could presumably account for them.]

L. P. Garrod

CHABBERT, Y. A. & PATTE, J. C. **Cellophane Transfer. Application to the Study of Activity of Combinations of Antibiotics.** *Applied Microbiol.* Baltimore, 1960, July, v. 8, No. 4, 193-9, 5 figs. [22 refs.]

This is a beautifully illustrated account [presumably the first to appear in the English language] of the transfer

method devised by Chabbert at the Pasteur Institute, Paris, for studying combined antibiotic action. A "tambourine" is prepared by stretching Cellophane over one side of a glass ring. The interior of this is inoculated by flooding and draining, and the device is then placed on a plate of nutrient medium on the surface of which antibiotic-containing paper strips have previously been placed at right angles and subsequently removed. Both nutrients and antibiotics diffuse through the Cellophane, and colonies develop on its exposed surface. After either 6 or 24 hours' incubation the tambourine is transferred to another plate of medium, free of antibiotic, to permit the growth of bacteria which have been inhibited but not killed. The advantage of the method over replica plating by means of velvet is that the whole population is transferred, and not merely a small fraction of it.

The nature of combined action is revealed by the distribution of colonies in the angle between the strips. Apart from well recognized appearances in this area denoting synergic, additive and antagonistic effects, other and more complex patterns are shown, including a symmetrical zone phenomenon, indicating that critical concentrations are more bactericidal than higher concentrations, and asymmetrical appearances showing that the relative concentrations of the 2 antibiotics determine their type of action.

The authors describe this as the most "sensitive" of all methods for studying combined action: it reveals effects which may be missed by the tube+plating method. Nevertheless when these 2 methods were compared in 208 tests the results were very rarely discordant (although some are described as "meaningless"—i.e., not distinctly indicating any type of combined action). There was more frequent discordance between the Cellophane tambourine method and replica plating by velvet. Some instances are given of how results so obtained can be applied therapeutically, including indications for only moderate dosage and against the use of a combination.

L. P. Garrod

SOUTHWAITE, A. H. & TRAFFORD, J. A. P. A New Synthetic Penicillin. *Brit. Med. J.* 1960, Sept. 3, 687-90. [11 refs.]

This is the first of a series of 7 papers in this issue about a new penicillin prepared from 6-aminopenicillanic acid by Beecham Research Laboratories. Hitherto known only as BRL 1241, this is now revealed to be sodium 6-(2,6-dimethoxy-benzamido) penicillinate monohydrate, and is to be known as Celbenin. This paper is purely clinical, and some background information, anticipating the contents of some of the succeeding papers, is necessary to an understanding of it. The outstanding property of Celbenin is total resistance to staphylococcal penicillinase, with the result that it is effective in penicillin-resistant staphylococcal infections. On the other hand its minimum inhibitory concentration for staphylococci is much higher than that of penicillin G for a sensitive strain, and the aim of treatment has therefore to be to maintain relatively high concentrations in the blood. In its instability in the presence of acid (necessitating parenteral injection), high solubility, rapid

absorption and renal excretion, and low toxicity, it closely resembles penicillin G.

These authors give the histories of 13 patients suffering from severe infections due to staphylococci resistant to penicillin G and other antibiotics, who were treated with Celbenin usually in doses of 1 gm. at 4-hour intervals. The infections were pneumonia (5), wound infections (4) and meningitis, extradural abscess, urinary tract infection and bronchiectasis (treated pre-operatively) in 1 each. All recovered except 1 patient who died of heart failure. It seems that the treatment consistently eliminated the staphylococcus from the site of infection. Some brief particulars are given of the blood levels attained. No serious side-effects were seen; some painful reactions occurred at injection sites, and a patient sensitive to penicillin G also manifested sensitivity to Celbenin by developing an extensive rash.

L. P. Garrod

KNOX, R. A New Penicillin (BRL 1241) active against Penicillin-Resistant Staphylococci. *Brit. Med. J.* 1960, Sept. 2, 690-93. [15 refs.]

This paper describes a laboratory study of the new penicillin, comparison being made with penicillins G and V and pheneticillin. Its minimum inhibitory concentration for staphylococci is about 2 μ gm./ml.; that for some other species, including streptococci and various Gram-negative organisms, is higher than that of other penicillins, notably penicillin G. Its action on resistant staphylococci, in contrast to that of other penicillins, is unaffected by inoculum size, and the presence of penicillinase [a commercial product of unstated derivation was used] does not interfere with its action. In a concentration of 5 μ gm./ml. it is bactericidal to both sensitive and resistant strains of staphylococci. It induces penicillinase formation in staphylococci forming this enzyme. On the other hand, an attempt to train a resistant strain to grow in higher concentrations of Celbenin resulted in loss of capacity to produce the enzyme.

L. P. Garrod

STEWART, G. T., with the technical assistance of Patricia M. HARRISON & R. J. HOLT. Microbiological Studies on Sodium 6-(2,5 Dimethoxybenzamido) Penicillinate Monohydrate (BRL 1241) *in vitro* and in Patients. *Brit. Med. J.* 1960, Sept. 3, 694-9, 6 figs.

This paper reports a further series of laboratory observations on the new penicillin. Sensitivity to it and to 3 other penicillins (as in the preceding paper) was tested by a disc method, the results being given simply as sensitive or resistant: all staphylococci and most streptococci were found sensitive and all Gram-negative bacilli except some strains of *Haemophilus* resistant. The rate of bactericidal action against several strains of staphylococcus exerted by different concentrations was measured: a bactericidal action on Group A streptococci was also demonstrated. In therapeutic tests in mice Celbenin (BRL 1241) was less effective against pneumococcal infection than penicillin G. Its resistance to

penicillinase (derived from 2 species of *Bacillus*) was confirmed. Attempts to train staphylococci to higher resistance to Celbenin had little effect.

Combinations of Celbenin with penicillin G and other antibiotics produced no enhanced effect. Some particulars are also given of blood levels attained in children during treatment with Celbenin and of the quantities excreted in the urine, amounting to about two-thirds of the dose given. An adult highly sensitive to penicillin G reacted locally with equal violence to a very small intradermal injection of Celbenin. *L. P. Garrod*

KNUDSEN, E. T. & ROLINSON, G. N. Absorption and Excretion of a New Antibiotic (BRL 1241).
Brit. Med. J. 1960, Sept. 3, 700-703, 2 figs.

This paper reports a pharmacological study of Celbenin by members of the staff of Beecham Research Laboratories. This form of penicillin is unstable in acid media and must therefore be injected. Its toxicity is very low: single intravenous doses of 2.5 gm./kgm. are tolerated by mice. Studies of absorption, distribution and excretion were made first with small doses in laboratory personnel, then in considerable detail in 3 patients: finally, when it appeared that a dose of 1 gm. at 4-hour intervals should suffice, this dose was given intramuscularly to 12 normal subjects. The average serum concentrations found after $\frac{1}{2}$, 1, 2, 4 and 6 hours were 17.6, 15.3, 5.3, 0.9 and 0.2 $\mu\text{gm./ml.}$: during this period 68% of the dose was excreted in the urine. [This rapid excretion of a large dose appears to correspond closely with the behaviour of sodium or potassium penicillin G.] *L. P. Garrod*

STEWART, G. T., NIXON, H. H. & COLES, H. M. T., with the collaboration of C. W. KESSON, D. LAWSON, R. G. THOMAS, J. N. MISHRA, M. EILEEN MITCHELL, J. MARJORIE SEMMENS & T. H. H. WADE. Report on Clinical Use of BRL 1241 in Children with Staphylococcal and Streptococcal Infections.
Brit. Med. J. 1960, Sept. 3, 703-6.

This paper describes the results obtained in infants and children from treatment with Celbenin, usually given in a total daily dose of 100 mgm./kgm. divided into 4 intramuscular injections at 6-hour intervals. There were 17 children with staphylococcal infection, most of whom had previously had unsuccessful treatment with penicillin G or other antibiotics. The diagnoses comprised septicaemia (2), osteomyelitis (1), abscess with possible underlying osteomyelitis (1), pneumonia (2), wound infections (4), skin infections (5) and throat infections (2). Only 2 patients died, 1 from intracranial haemorrhage and 1 owing to other underlying disease, and the staphylococcus was eliminated from all lesions and organs from which cultures were made after treatment, but not from carrier sites (nose and skin). The same treatment was tried in 12 cases of Group A streptococcal infection (9 throat, 1 otitis media, 1 impetigo and 1 wound infection). It was successful except in 2, the impetigo, which showed no response, and 1 tonsillitis which relapsed: both then responded to penicillin G. No side effects were seen

except pain and tenderness at injection sites: a few superinfections (coliforms or *Candida*) were observed.

L. P. Garrod

THOMPSON, R. E. M., WHITBY, J. L. & HARDING, J. W. Treatment of Experimental Penicillin-Resistant Staphylococcal Lesions with BRL 1241. *Brit. Med. J.* 1960, Sept. 3, 706-8, 3 figs. [10 refs.]

These experiments were done in mice, which received a large inoculum of staphylococcus culture into the thigh muscles, the result being judged by the degree of consequent inflammatory swelling, which was measured daily. The culture used was a type 80 strain of high mouse virulence, described as penicillin-resistant [it was "sensitive to 1.6 units/ml." but in the absence of information about the size of the inoculum used in determining this, the degree of its resistance remains conjectural]: other data show it to have been moderately resistant to streptomycin, highly so to tetracycline, and of approximately normal sensitivity to chloramphenicol, erythromycin and Celbenin. Each of these antibiotics was given in a single daily subcutaneous dose of 1 mgm. for 4 days. The order of therapeutic efficacy was erythromycin (much the most effective), chloramphenicol and streptomycin (equal), Celbenin (slightly less effective), penicillin G, tetracycline (both much less effective). In further experiments larger doses of Celbenin were used, and the best results were obtained with a single dose of 50 mgm.: this was more effective than 10 mgm. daily for 5 days. [The authors' conclusion is that "it is better to treat infections with a single overwhelming dose of this drug" is presumably not seriously intended to be acted on in the clinical field, especially since this dose is equivalent to nearly 200 gm. for a man of average weight.] *L. P. Garrod*

THOMPSON, R. E. M., HARDING, J. W. & SIMON, Rosemary D. Sensitivity of *Staphylococcus pyogenes* to Benzylpenicillin and BRL 1241. *Brit. Med. J.* 1960, Sept. 3, 708-9, 1 fig.

Of 1,118 strains of *Staphylococcus pyogenes* isolated from patients in the Middlesex Hospital, London, between June 1959 and April 1960 only 202 (18%) were sensitive to penicillin G, but all were sensitive to Celbenin, i.e., inhibited by concentrations of 1.6-3.2 $\mu\text{gm./ml.}$ *L. P. Garrod*

ROLINSON, G. N., STEVENS, Shirley, BATCHELOR, F. R., WOOD, J. C. & CHAIN, E. B. Bacteriological Studies on a New Penicillin—BRL 1241. *Lancet.* 1960, Sept. 10, 564-7, 1 fig.

This and the following, both from Beecham Research Laboratories, are companion papers in this journal to the series [see above] in the *British Medical Journal* about BRL 1241 (sodium 6-(2,6-dimethoxybenzamido) penicillinate monohydrate: Celbenin). Its minimum inhibitory concentrations are stated for a large number of

bacterial species, of which streptococci and other Gram-positive organisms seem rather less sensitive than to penicillin G (but comparative figures for these strains are not given) and various Gram-negative bacilli are much less sensitive. Staphylococci, regardless of their resistance to penicillin and other antibiotics, were regularly inhibited by 1.25 or 2.5 $\mu\text{gm./ml.}$ This is shown to be due to absolute resistance to staphylococcal penicillinase; on the other hand, slow inactivation is caused by *Bacillus cereus* penicillinase. Celbenin induces staphylococcal penicillinase formation. It completely inhibits the inactivation of penicillin G by *B. cereus* penicillinase but not by staphylococcal penicillinase. Celbenin is bactericidal to staphylococci in concentrations little above the bacteriostatic, and this action is unaffected by serum. It shows no synergy with penicillin G. Tolerance to Celbenin develops slowly during repeated transfer in media containing increasing concentrations: in parallel tests comprising 15 transfers the Oxford staphylococcus increased 500-fold in resistance to penicillin G and 10-fold to Celbenin.

L. P. Garrod

BROWN, D. M. & ACRED, P. **Chemotherapeutic Studies on a New Antibiotic—BRL 1241.** *Lancet.* 1960, Sept 10, 568–9, 2 figs.

This paper briefly reports experiments showing the lack of toxicity of Celbenin, and describes therapeutic tests in mice. In comparative tests with penicillin G against infection produced by intraperitoneal inoculation, neither had any action on infection by *Klebsiella pneumoniae* or *Salmonella typhi-murium*: the CD50 (mgm./kgm.) of Celbenin and penicillin G respectively for infection by a pneumococcus were 10.0 and 1.0 and by a sensitive staphylococcus 1.3 and 0.2; in infection by a resistant staphylococcus the CD50 of Celbenin was 100 and penicillin G was ineffective. The remaining experiments were in mice given an inoculation of staphylococcus culture into the thigh muscles and treated with 8 daily subcutaneous injections of 50, 100 and 200 mgm./kgm., the effect being judged by measurement of thigh diameter [this *Bulletin*, 1955, v. 30, 441]. Infection with a penicillin-resistant staphylococcus was favourably influenced by Celbenin to a degree proportional to the dose, but not by penicillin G, but the effect of the latter was decidedly superior against infection by a sensitive strain. It is mentioned [without details or evidence] in the "Conclusion" of the paper that large doses of Celbenin are required to ensure penetration into the cerebrospinal fluid, and that it does not combine with plasma protein to the same extent as penicillin G.

L. P. Garrod

MARTIN, W. J. & NICHOLS, D. R. **Penicillin V and Phenethicillin Potassium in Serum: Comparison of Concentrations and of Antibacterial Effects.** *Proc. Staff Meetings Mayo Clinic.* 1960, Sept. 28, v. 20, No. 35, 577–84. [12 refs.]

This comparison of penicillin V with potassium alpha-phenoxyethyl penicillin (phenethicillin) was made by

giving 4 250 mgm. doses of each at 6-hour intervals to 22 normal subjects and taking a single specimen of blood 2 hours after the last dose. The average amounts found in the serum were 1.65 and 2.67 $\mu\text{gm./ml.}$ of penicillin V and phenethicillin respectively. Dilutions of each serum were also inoculated with 3 strains of *Staphylococcus aureus*, incubated, and subcultivated to determine the minimum bactericidal dilution. One strain was apparently normally sensitive to penicillin, and the dilutions for both groups of sera, varying from 1:1 to 1:32, were bactericidal for it: the bactericidal dilution of sera containing penicillin V was greater than that of sera containing phenethicillin in 9 instances, the reverse in 9 and the same in 4. The 2 other strains were resistant, being inhibited by 50 $\mu\text{gm./ml.}$ penicillin V, and 12.5 and 25 $\mu\text{gm./ml.}$ of phenethicillin. Bactericidal effect by the sera was either absent or exerted at 1:1 or 1:2 (in 1 instance at 1:4): the differences favoured phenethicillin, sera containing this being more active in 9 instances against each organism, the converse being seen in only 2 and 4. [The authors refer to the fact that some of these sera were bactericidal in spite of containing less of the antibiotic than that found to inhibit growth in an ordinary sensitivity test, but they do not attempt to explain it. The size of the inoculum could do so: that for the serum tests was "at least 2,000 per milliliter", and that used for the determination of the minimum inhibitory concentration is not stated.]

L. P. Garrod

ENGLISH, A. R., MCBRIDE, T. J. & HUANG, H. T. **Microbial Resistance to Penicillin as related to Penicillinase or Penicillin Acylase Activity.** *Proc. Soc. Exper. Biol. & Med.* 1960, Aug.–Sept., v. 104, No. 4, 547–9.

Resistance to penicillin in some bacterial species depends on the formation of penicillinase, which converts penicillin into penicilloic acid. These authors claim to have shown that some strains of certain bacteria produce a penicillin acylase, the action of which on penicillin yields 6-aminopenicillanic acid: this has a very low activity compared with that of penicillin G against Gram-positive organisms, but a more nearly equivalent one against Gram-negative (minimum inhibitory concentrations for both against 18 species are given). Organisms found to form this acylase included several strains of *Escherichia coli*, *Klebsiella aerogenes*, *Pseudomonas pyocyanea* and *Proteus vulgaris*: on the other hand, other strains of all these species except the last formed penicillinase but not acylase. No organism formed both. Some resistant strains of 3 of these species formed neither.

L. P. Garrod

ANDO, K. **Effect of Streptomycin on Polynucleotide Phosphorylase from Avian Tubercle Bacilli.** *Nagoya J. Med. Sci.* 1960, Aug., v. 23, No. 1, 39–51, 10 figs. [21 refs.]

"The following results were obtained in a cell-free system on the depressing effect of streptomycin upon the synthesis of RNA, by using polynucleotide phosphorylase

prepared from avian tubercle bacilli and through the exchange reaction of ^{32}P .

"1) Streptomycin strongly depresses the activity of polynucleotide phosphorylase, *i.e.*, the incorporation ^{32}P into ADP.

"2) RNA is indispensable as a primer for polynucleotide phosphorylase. When YNA is given as a primer, the enzymatic activity is restored in spite of the co-existence of streptomycin.

"3) Streptomycin may not penetrate the cells of streptomycin-resistant bacilli, because it depresses the activity of this enzyme obtained from both sensitive and resistant strains.

"4) Inhibitory effect of streptomycin on the enzyme activity depends on the relative concentration of primer, RNA, and streptomycin."

ROSENBAACH, LOREN M., CAVILES, A. P. & MITUS, W. J. **Chloramphenicol Toxicity: Reversible Vacuolization of Erythroid Cells.** *New England J. of Med.* 1960, Oct. 13, v. 263, No. 15, 724-8, 6 figs. [20 refs.]

This paper concerns 2 patients, a woman given 4 gm. chloramphenicol daily for 16 days for pyelonephritis, and a girl aged 9 given the same dose for 18 days, together at times with streptomycin and sulphisoxazole, on account of pneumonia and empyema. In both patients the haemoglobin, leucocyte count and reticulocyte count fell during treatment (the last-named to zero in the first case), and marrow films showed a maturation arrest of the red cell series with the formation of numerous small vacuoles in the primitive red cells (referred to as "pronormoblasts"). There was also some vacuolization of granulocytes. Withdrawal of the drug was followed by erythroid hyperplasia, profuse reticulocytosis, and general restoration to normal. It is suggested that these marrow changes, of which there are several illustrations, are a useful sign of impending but reversible marrow damage by chloramphenicol. [Sternal puncture is a painful proceeding, and the idea that it should become a routine in patients given this drug is forbidding. The excellent charts of the blood pictures in these 2 patients suggest that the reticulocyte count should afford adequate warning.]

L. P. Garrod

ROLLY, H. & FUSSGÄNGER, R. Zur Wirkung der Tetracycline auf resistente Staphylokokken. [The Action of Various Tetracyclines on Staphylococci] *Deut. med. Woch.* 1960, Sept. 30, v. 85, No. 40, 1762-4, 1783-4, 1 fig.

This paper is from the Chemotherapeutic Institute of the firm of Hoechst, which markets pyrrolidinomethyl tetracycline as Reverin. The action of this form of tetracycline on staphylococci was compared with that of others both *in vitro* and *in vivo*. The order of simple inhibitory activity *in vitro* on 4 strains of staphylococci, 1 sensitive and 3 having different degrees of resistance, was chlortetracycline (most active), pyrrolidinomethyl tetracycline, tetracycline, oxytetracycline, with small differences. On the other hand, when mice were inoculated intraperitoneally with each of the 3 resistant

strains and given a single intravenous dose of 0.5 mgm 1 hour later, pyrrolidinomethyl tetracycline saved a majority of mice (about 60-95% to judge by the graphs of survival) from all 3 infections, whereas 75% or more died when treated with the other 3 tetracyclines. Blood assays at 5 time intervals after this dose showed that apart from low levels of chlortetracycline there was little difference between the concentrations attained and maintained up to 8 hours, and these were lower than the minimum inhibitory concentrations as determined *in vitro*.

L. P. Garrod

KNOTHE, H. **Demethylchlortetracycline: Laboratory and Clinical Studies.** *Antibiotic Med.* New York 1960, June, v. 7, No. 6, 349-57, 2 figs.

This paper from Kiel describes both a laboratory and a clinical study. Single or repeated doses of 20 mgm tetracycline or demethylchlortetracycline (DMCT) were given by stomach tube to numerous rabbits, pairs of which were killed after 3, 6, 12, 18, 24 and 48 hours in order to determine the antibiotic content of the liver, kidney, lung, brain, spleen, muscle and bone, aqueous humor, and bile, as well as the blood and urine. Tetracycline is poorly absorbed in rabbits (according to the text none was found in the serum after a single dose, but Table 1 contradicts this); this, combined with the fact that DMCT is more slowly excreted, is responsible for the organ levels of the latter being generally higher, particularly at the longer time intervals after a dose. Repeated doses of both antibiotics gave a cumulative effect. Assays of blood and muscle in 24-hour experiments in anaesthetized dogs gave similar results but with less pronounced differences owing apparently to the better absorption of tetracycline.

Assays of the antibiotic content of the blood in human beings were carried out at intervals after single and repeated doses of DMCT (there is a mistake in the legend of Fig. 1, which refers to repeated doses, although the curves evidently show the effect of single ones). Adequate therapeutic levels were maintained by a dose of 150 mgm. at 6-hour intervals or one of 300 mgm. every 12 hours, and it is mentioned that this dosage was found clinically effective in 65 patients.

L. P. Garrod

SWEENEY, W. M., DORNBUSH, A. C. & HARDY, S. M. **Antibiotic Activity in Urine and Feces after Oral and Intravenous Administration of Demethylchlortetracycline.** *New England J. of Med.* 1960, Sept. 29, v. 263, No. 13, 620-24, 5 figs. [17 refs.]

From among 27 subjects in whom the absorption of demethylchlortetracycline had been studied, 5 were chosen, 1 (A) attaining exceptionally high and 1 (E) an exceptionally low blood level after a single oral dose, the 3 others (B, C, D) being in the intermediate range. The blood levels attained in the subjects at 8 time intervals after a single dose are given. B, C, D and E were given a single oral dose of 150 mgm. and urine and faeces were collected for 104 hours and assayed. A excreted 43% in the urine and 23% in the faeces, E 9% and 72% respectively, the others having intermediate

values (it thus seems that some subjects consistently absorb this antibiotic much more or less than others). On the other hand, when the same intravenous dose was given to A, C, D and E, and the same assays were carried out, urinary excretion accounted for an average of 52% of the dose and the faecal for 6% with very little individual variation.

L. P. Garrod

KELLY, R. G. & BUYSKE, D. A. **Paper Chromatography of the Tetracyclines.** *Antibiotics & Chemotherapy*. New York. 1960, Oct., v. 10, No. 10, 604-7. [16 refs.]

VISCONTI, A. & GRASSI, L. *Studio in vitro sull'attività della Sigmanicina e dei suoi componenti su cento ceppi di stafilococco aureo. [In vitro Studies of the Action of Sigmamycin and its Components on 100 Strains of Staphylococcus aureus]* *Giorn. di Malattie Infettive e Parassit.* 1960, May-June, v. 12, Nos. 5/6, 269-84, 9 graphs & 6 figs. [40 refs.]

A translation of the author's summary is as follows:—The activity of Sigmamycin [which is a mixture of 2 parts of tetracycline and 1 of oleandomycin] was studied *in vitro* and compared with that of its components on 100 strains of *Staphylococcus aureus*. By using 3 different methods it was possible to confirm the synergic action between tetracycline and oleandomycin. This was observed in about 44% of strains examined, and more frequently in strains sensitive to oleandomycin than in those sensitive to tetracycline.

The authors compared the minimum bacteriostatic concentration of this combination with that of its components. Sigmamycin was shown to be more effective than tetracycline, and in strains sensitive to both components it was also more effective than oleandomycin. With strains resistant to tetracycline no difference was observed between Sigmamycin and oleandomycin.

The authors attempted to define the reasons for the discordant results obtained *in vitro* by various workers in the activity, efficacy and synergic action of Sigmamycin. They report observations arising from their own work and that of others, on the possible uses of Sigmamycin and its components.

Charles Wilcocks

ACOBSON, E. D., PRIOR, J. T. & FALLOON, W. W. **Malabsorptive Syndrome induced by Neomycin; Morphologic Alterations in the Jejunal Mucosa.** *J. Lab. & Clin. Med.* 1960, Aug., v. 56, No. 2, 245-50, 3 figs.

The oral administration of large doses of neomycin has been observed to cause steatorrhoea and deficient absorption of carbohydrates and other substances. In an endeavour to explain this, these authors obtained biopsies of the jejunal mucosa from patients treated with neomycin in preparation for abdominal operations. The operative series comprised 11 patients, all of whom had gastric operations (subtotal gastrectomy for ulcer in 8): 3 were given 4 gm. neomycin 3 times daily for 4 to 24 days before operation, and 1 had 4-8 gm. daily for 33

days: the remaining 5 were controls. Specimens were also obtained by means of a peroral jejunal biopsy capsule from 3 other patients, in one of them on 3 occasions, before, during and after neomycin treatment.

Sections of jejunal mucosa from treated patients, but not from controls, showed changes described as of the same nature, although less severe in degree, as those seen in non-tropical sprue: these were alteration in the shape of the villi, oedema, and infiltration with lymphocytes and plasma cells. In the single patient biopsied 3 times, the appearances had reverted to normal 18 days after treatment ceased.

[The histological appearances are illustrated, but cellular detail is indistinguishable in the photographs. The authors do not explain what purpose is supposed to be served by giving these large doses of neomycin for such long periods, particularly before operation on the stomach. An adequate degree of suppression of the flora of the lower bowel, which is the usual object of giving neomycin, can be achieved by giving neomycin for only 2 or 3 days and with smaller doses, particularly if combined with other appropriate measures.]

L. P. Garrod

KOOTA, G. M., SCHWEINBURG, F. B. & RUTENBURG, A. M. **Role of Kanamycin in the Management of Infections.** *New England J. of Med.* 1960, Sept. 29, v. 263, No. 13, 629-33. [34 refs.]

This is a general account of clinical experience with kanamycin, which was given intramuscularly, usually in doses of 0.5 gm. at 6-hour intervals for 2 days and at 12-hour intervals for a further 5 days, to 163 patients suffering from infections by staphylococci or coliform bacilli (*Escherichia*, *Klebsiella*, *Pseudomonas* or *Proteus* spp.). The principal conditions treated, with numbers of cases and recoveries, were general peritonitis (kanamycin also instilled intraperitoneally) 12 (12); septicæmia 10 (8); pulmonary infections (apparently mostly pneumonia, due in 9 cases to staphylococci) 17 (16); post-operative wound infections 36 (34); primary soft tissue infections 49 (39); urinary tract infections 33 (24). Of the 9 failures in the last category, 5 were infected with kanamycin-resistant coliforms, and 2 had "obstructive uropathy". Many assays of the antibiotic level in the blood were done at different intervals after a dose, the results of which are given in a large table: another table gives for a selection of 11 patients the diagnosis, clinical and bacteriological, the concentrations of kanamycin found in the blood and that found necessary to kill the organism *in vitro*, and the result.

Granular casts appeared temporarily in the urine of 13 patients and hyaline casts in several others [whether albuminuria also occurred is not stated]. An intravenous dose of 2 gm. daily for 12 days caused renal insufficiency and deafness in 1 patient; renal function returned to normal but hearing did not [no diagnosis or other particulars are given about this patient]. On the other hand, 21 patients had "impaired renal function or urinary-tract infection" before the antibiotic was given, and "in all 21 renal function improved". [According to table 3 total dosage varied in the whole series of patients from 5 to 19 gm.: the patient who became deaf after

2 gm. daily for 12 days, *i.e.*, a total of 24 gm., is therefore not accounted for here. It is clearly important to know how much kanamycin can be given without risk of damage to hearing.]

L. P. Garrod

TEJERINA, Genoveva & PORTOLÉS, A. A New Factor in the Use of Antibiotics. [Correspondence.] *Nature*. 1960, Oct. 8, v. 188, 155-6, 1 fig.

These workers in Madrid administered kanamycin to rabbits by injection for 1 month, the dose totalling 450 mgm./kgm., and then found that their serum contained a substance, absent from normal rabbit serum, which interfered with the action of kanamycin *in vitro*. The account of these tests is not clear, but it seems that solutions of the antibiotic which had been in contact with treated rabbits' serum for periods varying from 4 to 24 hours inhibited the growth of the Oxford staphylococcus in concentrations increasing from about 6 to 24 μ gm./ml., whereas in the absence of serum the minimum inhibitory concentration was 0.28 μ gm./ml. The nature of the interfering substance in such serum is unknown: it is said not to be a precipitin, but it fixes complement in the presence of kanamycin.

L. P. Garrod

LEVAN, N. E. Untoward Reaction to Griseofulvin. *Arch. Dermat.* 1960, Oct., v. 82, No. 4, 637.

"Following the administration of griseofulvin symptoms of headache, confusion, irritability, anorexia, tightness in the chest, and fatigue were noted. The causal relationship to the drug was established by repeated 'double blindfold' testing."

JENEY, E. & ZSOLNAI, T. Chemotherapeutische Studien in der Reihe der heterozyklischen Azo-Verbindungen. I. Aryl-azo-thiazole. [Chemotherapeutic Studies in the Series of Heterocyclic Azo-Compounds. I. Aryl-Azo-Thiazole] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 1, 84-95. II. Aryl-Azo-Derivate der N¹-Heterozykl-sulphonamide. [II. Aryl-Azo-Derivatives of N¹-Heterocycl-Sulphonamides] *Ibid.*, 96-112.

The English summaries appended to the papers are as follows:—

I. "The authors demonstrated different aryl-azo-derivatives of several N¹-heterocycl-sulphonamides and studied their bacteriostatic effect *in vitro* upon sulfanilamide-sensitive as well as resistant *Staphylococci* strains.

"The authors also studied the inhibition of their effect by means of p-amino-benzoic-acid, as well as the ability of beef serum to influence the bacteriostatic effect of the most effective compounds *in vitro*. p-Amino-benzoic-acid is not able to counteract the bacteriostatic effect of many prepared compounds. Those compounds whose effectiveness is not inhibited by p-amino-benzoic-acid, are also the ones that show an effect against sulfanilamide-resistant *Staphylococci*; but those whose effectiveness is counteracted by p-amino-benzoic-acid, show a bacteriostatic effect only against sulfanilamide-sensitive strains.

"The bacteriostatic effect observed here is not caused by the counterplay with p-amino-benzoic-acid but by some other biochemical mechanism. Neither the compounds demonstrated by the authors, nor the sulfanilamides used as comparison were bacteriostatically effective against Gram-negative micro-organisms.

"As the bacteriostatic effect *in vitro* of the most effective compounds is strongly lessened by serum, and since they are not absorbed from the digestive tract, the authors do not consider it probable, that any of these compounds are useful for internal treatment of general *Staphylococcus* infections. Experiments in the local therapy of *Staphylococcal* pyodermias or mucous membrane and ear inflammations might be worthwhile with the most effective compounds as 4-Tolyl-azo-4-Chlor-phenyl-azo-, and 4-Chlor-azobenzol-4'-azo-derivatives of ultraseptyl (No. 8., 9., 31.) as well as 4'-Tolyl-azo- and 4'-Chlor-phenyl-azo-derivatives of 4-Phenyl-sulphathiazole (No. 44 and 45).

II. "The authors have synthesized 14 aryl-azo-thiazole derivatives, two aryl-azo-pyridin-derivatives, and one aryl-azo-imidazol-derivative. They studied their bacteriostatic effect *in vitro* on polyresistant *Staphylococcus aureus* and *albus* strains, as well as on twenty different Gram-negative bacteria strains. The 5-4'-Tolyl-azo- and the 5-4'-chlor-phenyl-azo-derivative of the 2-amino-4-methyl-thiazols proved most effective against the *staphylococcus* strains. These, as well as the other combinations studied were totally ineffective against Gram-negative bacteria. The authors discussed the relationships between the chemical structure and the bacteriostatic effect in the series of aryl-azo-thiazole.

"The bacteriostatic effect of the two most effective aryl-azo-thiazol-derivatives mentioned on *Staph. aureus* and *albus* strains *in vitro* is cancelled by serum, or, at least, decreased to a great degree. For this reason, the authors are of the opinion that these are unsuitable for treatment of internal *staphylococcus* infections. On the other hand, therapeutic experiments might be made in the local treatment of pyodermias."

JENEY, E. & ZSOLNAI, T. Über die bakterio-statische Wirkung einiger Substitutionsprodukte des Sulfathiazols und seiner Derivate. [On the Bacteriostatic Effect of Several Substitute Products of Sulphathiazole and its Derivatives] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 1, 113-17.

The English summary appended to the paper is as follows:—

"The authors demonstrated the bromized, iodized and nitrized derivatives of several sulfathiazoles and studied their bacteriostatic effect *in vitro*. It was found that the demonstrated compounds act bacteriostatically only on sulfanilamide-sensitive *Staphylococci* strains; on the other hand they are without any effect on sulfanilamide-resistant *Staphylococci* strains as well as on Gram-negative bacteria. The bacteriostatic effect of these compounds on sulfanilamide sensitive *Staphylococcus* strains could be counteracted by p-amino-benzoic-acid; because of this, the authors concluded, the mechanism of the bacteriostatic effect of the demonstrated bromized

iodized, and nitrized sulfathiazole derivatives is identical with that of the respective non-substituted sulfathiazoles."

BARRY, V. C., BUGGLE, Katherine, BYRNE, Joan, CONALTY, M. L. & WINDER, F. **Absorption, Distribution and Retention of the Rimino-Compounds in the Experimental Animal.** *Irish J. Med. Sci.* 1960 Aug., 6th Ser., No. 416, 345-52. [12 refs.]

Certain rimino compounds have been shown by these authors and others to possess high activity against tubercle bacilli both *in vitro* and experimentally *in vivo* [this *Bulletin*, 1957, v. 32, 945]. They are in general highly fat-soluble but some have very low solubility in water. This paper is concerned with the distribution of 2 of these compounds when administered orally to mice, rats and rabbits. After some days of treatment increasing quantities of the drug were found to be present in the liver, lungs and spleen, which persisted there after treatment was stopped (evidently accounting for the fact that a single dose can greatly prolong survival during tuberculous infection). One of the compounds, which is water-insoluble, also accumulated in the body fat. Only tentative attempts have so far been made to determine how these compounds behave in man. *L. P. Garrod*

HANKA, L. J. **Mechanism of Action of Psicofuranine.** *J. Bacteriology.* 1960, July, v. 80, No. 1, 30-36, 3 figs. & 1 diagram. [19 refs.]

Psicofuranine is a recently described antibiotic possessing anti-bacterial (and anti-tumour) activity *in vivo* but no anti-bacterial activity *in vitro* as demonstrable by ordinary methods. It nevertheless inhibits the growth of *Staphylococcus aureus* on a special medium for the composition of which the reader is referred to a previous paper [this *Bulletin*, 1959, v. 34, 1156]. The purpose of the present one is to report that this inhibitory action is prevented by the addition to the medium of guanine and related compounds, and to a much less extent by adenosine. This effect was examined quantitatively by including different amounts of these substances in a solid medium and measuring the inhibition zones produced by discs containing different quantities of the antibiotic. It thus appears that psicofuranine, the structure of which resembles adenosine, has an anti-metabolite action, the interference being with purine metabolism and thus with the synthesis of nucleic acid. *L. P. Garrod*

RALSTON, D. J. & ELBERG, S. S. **Action of Glycine and a Lysozyme-Like Agent from Rabbit Monocytes in Destruction of *Brucella*.** *Proc. Soc. Exper. Biol. & Med.* 1960, July, v. 104, No. 3, 464-7, 3 figs.

Extracts of rabbit monocytes appear to contain an agent which resembles a lysozyme. Living brucellae are very resistant to the action of this agent but when treated with glycine the bacterial cells are no longer resistant to its action and they are lysed. The agent can be extracted from rabbit monocytes by freeze-thawing or by Mickle

disintegration in phosphate buffer or in distilled water, and yields from $2-3 \times 10^8$ monocytes exhibited lysozyme activity for *Micrococcus lysodeikticus* comparable to concentrations of crystalline egg-white lysozyme (Worthington) in the order of 500 μgm . When cultures of these monocytes are parasitized by a strain of *Brucella melitensis* and treated with low concentrations of glycine it is found that the intra-cellular growth of the organisms is suppressed. It is suggested that the intraphagocytic death involves a stepwise alteration of the bacterial cell-wall, followed by enzymatic degradation of the mucopolysaccharide component responsible for the structural integrity of the organism. *H. J. Bensted*

WRIGHT, Eleanore S. & MUNDY, R. A. **Defined Medium for Phenol Coefficient Tests with *Salmonella typhosa* and *Staphylococcus aureus*.** *J. Bacteriology.* 1960, Aug., v. 80, No. 2, 279-80.

LOWBURY, E. J. L., LILLY, H. A. & BULL, J. P. **Disinfection of the Skin of Operation Sites.** *Brit. Med. J.* 1960, Oct. 8, 1039-44. [12 refs.]

Delimited areas of normal skin were contaminated with a penicillin-resistant staphylococcus, treated with antiseptics, and sampled by applying a glass cylinder, introducing 5 ml. of fluid containing an appropriate neutralizer and rubbing the skin beneath this: the fluid was then diluted and cultivated in plates of nutrient agar containing penicillin (this is the method originally devised by STORY [this *Bulletin*, 1953, v. 28, 209]. No staphylococci were recovered after 2 minutes' (a few in some cases after 20 seconds') treatment with 70% alcohol, iodine 1% in 70% alcohol, 2% aqueous iodine, "virac" (an iodophor) or 0.5% chlorhexidine in 70% alcohol. On the other hand there were survivors after treatment with 2% aqueous cetrimide, and many more after 0.1% Penotrane (phenyl mercuric dinaphthylmethane sulphonate). These substances were therefore not tested further. It was shown in tests by the same technique that alcoholic solutions of both iodine and chlorhexidine will also eliminate *Pseudomonas pyocyanea* applied to the skin surface.

A further series of tests was designed to ascertain the effect of antiseptics on the resident as distinct from the transient flora. Hands were first washed and dried on a sterile towel, sampled by rubbing together in a basin of sterile Ringer's solution containing neutralizers which was then cultivated quantitatively, treated with antiseptic, and sampled in the same way again. The mean (of many observations) percentage reductions in count were alcoholic chlorhexidine 81.3, alcoholic iodine 80.7, alcohol 68.6, aqueous iodine 67.4, aqueous chlorhexidine 60.7 and Virac 58.3 (control 14.7). When hands were repeatedly treated with alcohol no further effect was obtained by treatments continued after the 2nd. It was also found that when both total bacteria and *Staph. aureus* were enumerated after treating nurses' hands with alcohol, both counts fell proportionately, suggesting that *Staph. aureus* may be present in the deeper layers of the skin. *L. P. Garrod*

CLAUBERG, K. W. Versuche zum Ersatz der Dampfdesinfektion durch gezielt strömende Entkeimungsgase. I. Mitteilung: Wirksame Anwendung von Triäthylenglycol im TCP-Gerät. [Studies of the Substitution for Steam Disinfection of a Directed Flow of Bactericidal Vapour] *Arch. f. Hyg. u. Bakt.* 1959, Nov., v. 143, No. 7, 491-4.

This paper points out the need for disinfecting bedding and mattresses in the prevention of hospital infection, and discusses the efficacy and drawbacks of some methods of achieving it. The "TCP" apparatus was used for the experiments described: this is apparently a well known piece of equipment in Germany commonly employed for disinfection by steam [the initials represent the names of the authors Trautmann, Clauberg and Pflanz]. The author raised the temperature of the chamber to 100°C. and admitted triethylene glycol vapour. *Staphylococcus aureus* and *Escherichia coli* were killed in 30 and 20 minutes respectively if fully exposed and in 70 and 60 minutes if inside mattresses. The method was relatively ineffective against spores, but the author points out that this rarely matters. [No description of the apparatus is given, nor is anything said about the concentration of triethylene glycol vapour required to produce the effects described.]

L. P. Garrod

RUBBO, S. D., STRATFORD, B. C. & DIXSON, Shirley. "Self-Sterilization" of Chemically Treated Blankets. *Med. J. Australia.* 1960, Aug. 27, v. 2, No. 9, 330-32, 1 fig.

A number of chemical processes have been described for the "sterilization" of blankets [this *Bulletin*, 1955, v. 30, 897; 1959, v. 34, 807]—recently it has been claimed

that residual antibacterial activity makes the blankets virtually self sterilizing [*ibid.*, 1958, v. 33, 63]. The present paper describes experiments made to test this point by using four chemicals—Hibitane (1 in 1,000), Fixanol C, Cirrasol OD, and Permachem. 3 types of test were used. First, pieces of treated blanket were placed on a lawn plate of *Staph. aureus* and zones of inhibition were measured. All four of the chemicals tested produced zones, varying from 2 to 15 mm. Untreated blanket produced no inhibition.

Secondly, blanket strips were contaminated with *Staph. aureus* and immediately cultured in broth and broth containing Lubrol and lecithin as neutralizers. All 44 chemically treated blankets yielded growth from the neutralizer broth only, indicating that considerable bacteriostatic activity was transferred with the blanket.

In the third series of tests, strips of treated blankets were sown on to blankets in use by patients: after 30 days' use the exposed surfaces of the strips were sampled by contact plates and by a percussion method. In each case the results were the same as from an untreated control strip when medium containing neutralizer was used. In ordinary broth, however, no growth occurred.

The authors conclude that these results "do not support the view that chemically sterilized blankets possess the unique property of remaining sterile during use". They consider that this failure to remain sterile is due to the mechanism of natural contamination by air-borne organisms as free particles or "fibre nuclei". "... in the absence of an aqueous vehicle it is impossible for a chemical adsorbed on a woollen fibre to establish effective contact with an air-borne organism which may settle on it."

[This paper emphasizes the point that the real problem is not how to render blankets bacteriologically clean, but how to prevent the recontamination which takes place within a day or two of their use in the ward.]

J. C. Kelsey

BACTERIA

The order in this section is:—Cocci; *Donovania*; *Mycobacterium*; *Corynebacterium*; *Haemophilus*; *Pseudomonas*; *Pfeifferella*; *Enteric Organisms*; *Brucella*; *Pasteurella*; *Bacillus*; *Anaerobes*; *Spirochaetes*; *Erysipelothrix*; *Listeria*; Others.

MÄKELÄ, P. Studies on *Staphylococcus aureus* in Helsinki. The Distribution of Phage Types and Antibigrams, and their Association with Certain Other Characteristics. *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, Suppl. 1, 85 pp., 3 figs. [168 refs.]

This work reports the results of investigations into the prevalence, phage type and antibiotic pattern of *Staphylococcus aureus* isolated between October 1958 and July 1959, in the absence of any epidemic, in Helsinki hospitals and from people living in that town. The results are preceded by a very comprehensive and useful review of the literature.

There were 14,000 cultures consisting of:—

1. Nose and/or throat swabs from 699 normal adults, 597 normal children, 180 members of 27 families, 875 members of hospital personnel, and 1,845 in-patients in hospital taken on admission or discharge.
2. Skin swabs from 384 infants on admission or during stay in hospital.
3. Pus swabs from 845 staphylococcal lesions.
4. Specimens from pharynx, faeces or sputum from 741 patients with no apparent staphylococcal disease.
5. 291 strains from pus from other sources.

Normal adults had a nasal carrier rate of 40% and children of 60%. 51% of 667 hospital personnel examined were constant staphylococcal carriers, 22%

were persistently negative. Skin carriage in normal infants was 53%.

In a total of 4,539 independent strains, 31 different phage types were distinguished, the commonest being 52/52A/80 (10%) but 20 strains each accounted for more than 1% of the total (these were types which have been found to be common in other countries). There was a tendency for members of a family to carry strains of the same type and strains were isolated from 2 sites of the same person 685 times; they were always of the same type and 2 out of 3 of them were of the same antibiotic pattern.

Of the strains from normal adults 30% were resistant to penicillin but 94% of strains from infants under 1 year were resistant to penicillin and 39% to tetracycline. These figures were 37% and 5.8% respectively in non-hospital children between 4 and 15 years of age. 70% of strains from hospital personnel and 61% of in-patient strains were resistant to penicillin, the figures for tetracycline were 23% and 33% respectively.

More than 90% of multiply-resistant strains belonged to one of 5 phage types, and strains of these types and patterns were isolated from all hospitals examined. [They are the well-known epidemic types.]

M. Patricia Jevons

PULVERER, G. & GRÜN, L. Untersuchungen zur Differenzierung des Staphylokokken-Standardstammes "SG 511". [Investigations on the Differentiation of the Standard Staphylococcus Strain SG 511] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 6, 537-43.

Staphylococcal cultures with the strain number SG 511 have been widely used in Germany for antibiotic sensitivity testing and the like. Strains from 8 different institutes differed greatly in phage and serological types, antibiotic sensitivity, and enzyme production. (See also POHN, *Zent. f. Bakt., I. Abt. Orig.* 1960, v. 177, 432.)

R. E. O. Williams

DINEEN, P. Effect of Reduction of Bowel Flora on Experimental Staphylococcal Infection in Mice. *Proc. Soc. Exper. Biol. & Med.* 1960, Aug.-Sept., v. 104, No. 4, 760-62, 2 figs.

"Survival and microbial population studies in mice with their intestinal flora reduced by neomycin indicate that these animals are much more susceptible to intravenous staphylococcal infections than their littermate controls."

SUGIYAMA, H., BERGDOLL, M. S. & DACK, G. M. *In vitro* Studies on Staphylococcal Enterotoxin Production. *J. Bacteriology.* 1960, Aug., v. 80, No. 2, 265-70, 2 figs. [14 refs.]

The authors present an *in vitro* method for demonstrating staphylococcal enterotoxin production. A purified enterotoxin was prepared from an enterotoxin-producing strain (S-6), and used to immunize rabbits. The Gamma

globulin fraction of this serum produced 2 precipitin bands when tested with crude S-6 enterotoxin. Absorption of the serum with a non-enterotoxic strain of staphylococcus resulted in a preparation which gave 1 precipitation line only, with crude and purified S-6 enterotoxin.

This serum was incorporated into amigen agar plates in final concentrations of 1:2 and 1:4. S-6 culture streaked on these plates gave colonies after 48 hours, some of which were surrounded by large haloes of precipitation, other colonies had smaller haloes and some produced none. Colonies of each type were grown in fluid medium and the amounts of enterotoxin in the supernatants were compared in Oudin tubes. Results showed that colonies varied in the amount of enterotoxin they produced and there was a correlation between this and the size of the halo. Supernatants of some colonies producing no haloes on plates produced no precipitation bands by Oudin technique even when concentrated 10 times.

The double diffusion technique was suitable for testing 6 strains on a plate. Antigen reservoirs filled with S-6 antigen were placed between test strains in a row, with a row of antiserum-containing wells below. When adjacent colonies produced antigen of S-6 type, precipitation lines joined with the line produced with the purified S-6 antigen. Of 29 strains tested by this means none of the 8 which were non-enterotoxigenic by monkey-feeding tests produced precipitin lines. Of the 21 strains toxic to monkeys 10 showed reactions of identity with S-6 enterotoxin and produced haloes on serum plates. 11 showed no precipitin lines when tested against S-6 antiserum.

Results suggest that there are at least 2 different antigenic types of enterotoxin.

M. Patricia Jevons

MESROBEANU, I., GEORGESCO, M., IEREMIA, T., MITRICĂ, Natalia, DRĂGHICI, Domnica & MATEESCO, Maria. Action des toxines microbiennes sur les cultures de tissus. I. Action de l'Alpha-toxine staphylococcique sur les cultures de tissu embryonnaire humain. Essais de titrage. [The Action of Microbial Toxins on Tissue Cultures. I. The Action of Staphylococcal Alpha-Toxin on Human Embryo Tissue Cultures. Attempts at Quantitative Assay] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, June, v. 19, No. 2, 161-71, 9 figs. [19 refs.]

Tissue cultures were grown from human embryos and tested for susceptibility to preparations of staphylococcus alpha toxin. The minimum cytotoxic dose was found to be about 2.5 Lf, when determined either by titration with toxin of known strength or by an antiserum neutralization method.

R. E. O. Williams

SMITH, H. W. & CRABB, W. E. Antibiotic Sensitivity of Staphylococci from Noses of Veterinary Surgeons and Farmers. *Lancet.* 1960, Sept. 3, 515-16.

Nasal swabs were obtained from 200 veterinary surgeons and 200 farmers and cultivated in 8% sodium chloride meat broth which was then plated: multiple

coagulase-positive colonies were then examined for antibiotic sensitivity and other properties. The percentages of carriers of coagulase-positive strains were 34% in veterinary surgeons and 38% in farmers; of these strains 88 and 21% respectively were resistant to penicillin and 15 and 3% to tetracycline, streptomycin or chloramphenicol. Reasons for this difference are discussed, and that favoured is the simple one that veterinary surgeons frequently handle antibiotics. The alternative possibility that the organisms are derived from treated animals is rejected because "contact between veterinary surgeons . . . and their patients receiving penicillin is infrequent and brief compared with the contact medical and nursing staffs of hospitals have with theirs". [This is an interesting view which no one outside the veterinary world should perhaps dispute, but it may be pointed out that if veterinary surgeons themselves inject penicillin into the teat canals of cows, this amount of "contact" should be quite enough to transmit infection.] *L. P. Garrod*

HALL, W. H. **Rate of Development of Resistance in *Staphylococcus aureus* to Erythromycin in Combination with Oleandomycin, Vancomycin, or Dihydrostreptomycin.** *J. Lab. & Clin. Med.* 1960, July, v. 56, No. 1, 83-104, 15 figs. [16 refs.]

This paper records a large number of experiments in which small numbers of strains of *Staph. aureus* were "trained" to grow in increasing concentrations of various antibiotics; the rate of acquisition of resistance was measured for the antibiotics taken singly and in combination. Resistance to penicillin was developed slowly and often limited by the appearance of small-colony variants. On the other hand most strains could be rapidly adapted to neomycin and dihydrostreptomycin. Some strains adapted readily to erythromycin and one to vancomycin. In general the rate of adaptation was less when combinations of antibiotics were used.

R. E. O. Williams

GRÜN, L. & ARNOLD, G. **Über die antibakterielle Staphylokokken-Immunität. [Antibacterial Staphylococcal Immunity]** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 6, 481-8, 3 figs. [13 refs.]

Batches of 5 rabbits were immunized with washed suspensions of *Staphylococcus aureus* treated in various ways and were subsequently challenged with a large dose of staphylococci. In most cases all the unimmunized rabbits died within 4 weeks. Formalinized vaccines gave better protection than autoclaved. There was some degree of cross-protection between strains of different serological type, to explain which the existence of a new antigen "m" is postulated.

R. E. O. Williams

MOUSTARDIER, G., DULONG DE ROSNAY, C., DU PASQUIER, P. & LATRILLE, J. **Un milieu simple pour l'isolement des streptocoques. [A Simple Medium for Isolation of Streptococci]** *Ann. Inst. Pasteur.* 1960, Sept., v. 99, No. 3, 444-6.

Kanamycin (25 μ gm. per ml.) and mycostatin (2 μ gm. per ml.) can be incorporated in blood agar plates to

serve as useful selective agents in the isolation of haemolytic streptococci.

R. E. O. Williams

KOMINE, I., SLADE, H. D. & HESS, E. L. **The Separation and Some Chemical, Physical and Biological Properties of a Nucleoprotein from *Streptococcus pyogenes*.** *Arch. Biochemistry.* 1960, Aug. v. 89, No. 2, 245-52, 2 figs. [29 refs.]

EKSTEDT, R. D. & STOLLERMAN, G. H. **Factors affecting the Chain Length of Group A Streptococci. I. Demonstration of a Metabolically Active Chain-Splitting System.** *J. Exper. Med.* 1960, Oct. 1, v. 112, No. 4, 671-86, 5 figs. [24 refs.] **II. Quantitative M-Anti-M Relationships in the Long Chain Test.** *Ibid.*, 687-98. [12 refs.]

(i) MALESCHKOFF, B. **Über eine verbesserte Methode der Antistreptolysinbestimmung. [An Improved Method for Antistreptolysin Titration]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, July, v. 6, No. 7, 445-7.

(ii) RUDOLPH, F. **Eine vereinfachte Methodik der Antistreptolysinreaktion. [A Simplified Method for the Antistreptolysin Reaction]** *Ibid.*, 447-51.

These two papers describe modifications of Kalbak's antistreptolysin titration methods. The first consists of an increase to 0.2 ml. of the volume of fluid in which the streptolysin is added. The second also includes modifications to reduce pipetting errors and recommends the use of automatic pipettes. Details must be sought in the original.

R. E. O. Williams

SCHMIDT, W. C. **Type-Specific Antibody Formation in Man following Injection of Streptococcal M Protein.** *J. Infect. Dis.* 1960, May-June, v. 106, No. 3, 250-55. [12 refs.]

M protein was extracted from the cell walls of a strain of *Streptococcus pyogenes* (Lancefield type 19) at pH 2 at 95°C. It was further purified by acid precipitation, ribonuclease digestion and ammonium sulphate fractionation. Saline solutions of this purified material, either free or in combination with aluminium phosphate, were injected into 3 groups of subjects:

(A) 2 men, who tolerated well subcutaneous injections in doses of 10 to 80 μ gm. of the material;

(B) 12 men, 7 of whom did not have initially type 19 bactericidal antibody in their sera; after receiving 3 subcutaneous doses 3 to 4 weeks apart the serum of 2 of these 7 now had type 19 bactericidal antibody;

(C) 23 children, none of whose sera initially contained type 19 bactericidal antibody. Each child received 6 intramuscular injections of the aluminium phosphate type 19 M protein preparation. 3 children had developed type 19 bactericidal antibody in their sera 4 months after the first injection; in one child the antibody was still present 5 months later.

H. Gooder

RAVIN, A. W. **Linked Mutations borne by Deoxyribonucleic Acid controlling the Synthesis of Capsular Polysaccharide in *Pneumococcus*.** *Genetics*. 1960, Oct., v. 45, No. 10, 1387-404, 2 figs. [18 refs.]

COLETSOS, P. J., with the technical collaboration of E. ORIOU & N. DE REGEL. Milieux et modalités de culture adaptés à la réanimation et à la multiplication *in vitro* de *Mycobacterium tuberculosis* de vitalité réduite, de viabilité éphémère, ou en état de quiescence. [Media and Methods of Culture adapted to the Reanimation and Multiplication *in vitro* of *Mycobacterium tuberculosis* of Reduced Vitality, Ephemeral Viability or in a State of Quiescence] *Ann. Inst. Pasteur*. 1960, Oct., v. 99, No. 4, 475-95, 1 text fig. & 8 figs. on 4 pls. [28 refs.]

The first part of this lengthy article is a review of the conditions that may lead to the state in which tubercle bacilli remain viable in tissues but cannot be grown on the routine media. The remainder of the article describes in detail media used at the Institut Pasteur in which are grown tubercle bacilli that do not grow on Jensen medium. No figures are given to support the claim, but there are photographs of cultures from 6 patients and these show no growth on the standard medium but very definite growth on the modified media.

Three media are described, and they are all prepared from the same basal medium. This is an egg medium with the special additives, sodium pyruvate, sodium glutamate, blue litmus from lichens, ossein (gelatin) and number of trace metals.

The basal medium is suitable for the growth of the so-called normal bacilli and it gives more luxuriant growth than does Jensen medium. For tubercle bacilli of extra-pulmonary sites and biopsy specimens, the concentration of ossein is increased from 4 to 20%. This concentration ensures that there is about 0.3 ml. of free ossein in the tube and if the inoculum is introduced in this, the tubercle bacilli are protected from direct contact with air during their initial stage of growth—a condition which the author maintains encourages the growth of quiescent bacilli.

For tubercle bacilli in a state of reduced vitality the surface of either the basal medium or the basal medium with ossein is flooded with an extract of the liver of a monkey.

The author also emphasizes that for successful cultivation of the bacilli of reduced vitality the administration of antibiotics to the patient should be suspended for a day before the specimen is collected, the specimen must be fresh, the homogenization and the centrifuging of the specimen should be minimal, and the tubes of media should be capped and incubated in the horizontal position.

S. R. M. Bushby

LEGOMMIER, J. Contribution à la connaissance du mode de multiplication du bacille tuberculeux. Les bacilles acidophiles. [Contribution to the Study of the Mechanism of Tubercle Bacillus Multiplication. Acidophilic Bacilli] *Ann. Inst. Pasteur*. 1960, Nov., v. 99, No. 5, 767-76, 2 figs. on pl. [11 refs.]

SUBBAIAH, T. V. SELKON J. B., BHATIA, A. L., MITCHISON, D. A. & RADHAKRISHNA, S. The Addition of Para-Aminobenzoic Acid or Catalase to Löwenstein-Jensen Medium and the Effect of Prolonged Incubation in the Culture of Tubercle Bacilli. *Tubercle*. 1960, Oct., v. 41, No. 5, 334-40. [19 refs.]

The addition of 10 μ gm. PABA per ml. to Löwenstein-Jensen medium, without potato starch, was shown not to increase the number (528) of positive cultures or the amount of growth from 1,792 sputa from patients undergoing isoniazid-PAS treatment. This failure to improve the results by adding PABA was attributed to the dilution of the PAS in the sputum during the washing of the centrifuged deposit of the specimen after treatment with sodium hydroxide. Similarly, addition of 2 μ gm. catalase to the tubes of media did not increase the 818 specimens yielding positive cultures from the total number of 2,814 specimens. Extension of the incubation period from 8-9 weeks to 16-17 weeks increased the positive specimens from 1,138 sputa from 39.1% to 39.5%.

S. R. M. Bushby

LLOYD, Janet. A Method for studying Micro-Colonial Structure and Cord Formation. *Tubercle*. 1960, Aug., v. 41, No. 4, 281.

A suitable method for the study of micro-colonial structure and cord formation should not cause disturbance of the micro-colonial structure, such as occurs when growth is transferred from a liquid medium to a slide [this *Bulletin*, 1952, v. 27, 888] and it should allow the organisms to be stained, which cannot be done in the agar block method [*ibid.*, 1953, v. 28, 983]. Slide cultures [*ibid.*, 1951, v. 26, 1027] do allow undisturbed colonies to be stained, but not all strains grew satisfactorily in them. Growth on membrane filters [*ibid.*, 1955, v. 30, 1106] also allows staining of undisturbed micro-colonies, but the present author, from the MRC unit for Research on Drug Sensitivity in Tuberculosis, London, describes a simpler method.

3-4 mgm. of a 2-3-week old culture of the strain to be studied, on Löwenstein-Jensen medium, is shaken with 0.4 sterile distilled water in a screw-capped bottle with glass beads. The suspension is diluted by adding 0.1 ml. to 5 ml. of Kirchner medium without penicillin. A drop of this dilution is placed on a sterile slide where the area of growth is confined by a ring of soft petroleum jelly 10-15 mm. in diameter. The slide has previously been set on a 1% aqueous agar plate. The plate is incubated at 37°C. in a polythene bag sealed by heat, so that evaporation of the drop is prevented. After 5, 7 or 14 days incubation the slides are exposed to ultra-violet light (3 ft. from a Philips TUV 30 watt germicidal strip light) for 30 minutes. They are then passed in series through Coplin jars containing (1) ethanol for fixation (15 minutes); (2) xylol, to remove the vaseline (15 minutes); (3) ethanol (2-3 secs.); (4) stains such as those for the Ziehl-Neelsen method. Cord formation was seen with tubercle bacilli treated in this way in an early stage after 5 days incubation and was well marked

after 7 days. With strains of *Nocardia*, the micro-colonial morphology remained undisturbed throughout. The drops of Kirchner medium did not evaporate even after 14 days.

H. J. O'D. Burke Gaffney

GUTIÉRREZ-VÁZQUEZ, J. M. Prueba de mancha en papel filtro para la diferenciación química de bacilos tuberculosos humanos con respecto a otros mycobacteria. [Filter Paper Spot Test Method for the Chemical Differentiation of Human Tubercle Bacilli from Other Microbacteria] *Rev. Latinoamer. Microbiol.* Mexico, 1960, Mar., v. 3, No. 1, 41-5, 1 fig. English summary.

In this method 0.5 ml. of water is added to a well grown culture of the bacilli on Löwenstein-Jensen medium and then autoclaved. A sufficient quantity of the water is then placed on filter paper to give 2 spots, 20 mm. in diameter, and after they have dried a second quantity is added to one of them. When dry the paper is sprayed with a 1.5% alcoholic solution of orthotolidine and 30-40 seconds later it is placed in a chamber saturated with BrCN. This reagent should be placed in the bottom of the chamber and should not touch the paper. With human tubercle bacilli an intense pink colour develops in 8-10 minutes, due to the presence of significant quantities of niacin, and with other varieties the spots remain either white or at the most turn a pale rose. With poorly grown human strains the colour may develop in only the double spot. S. R. M. Bushby

NASTA, M., PAUNESCO, E. & GEORGESCO, P. Modifications métaboliques et pouvoir pathogène de *Mycobacterium tuberculosis*. [Metabolic Alterations and Pathogenicity of *Mycobacterium tuberculosis*] *Ann. Inst. Pasteur.* 1960, Oct., v. 99, No. 4, 504-22. [28 refs.]

With the Warburg apparatus H37Rv was shown to metabolize, especially under aerobic conditions, all the constituents of the Krebs' cycle as well as acetate and its precursors (pyruvate, lactate, citrate, leucine and isoleucine). The presence of 100 µgm. isoniazid per ml. prevented the metabolism of citrate, cetoglutarate, fumarate, acetate, lactate leucine or isoleucine, but it had no action on that of malate, oxalo-acetate or succinate, although it stimulated the decarboxylation of pyruvate; the presence of co-enzyme I did not reverse the inhibitory action. Although they were less active H37Ra and BCG showed in general similar qualitative metabolic processes as H37Rv but they could not utilize citrate, cetoglutarate or malate, and in the case of H37Ra leucine or isoleucine.

The metabolism of variants of H37Rv and BCG, resistant to 100 µgm. isoniazid per ml., were similar to those of the avirulent strains except that they were unaffected by the presence of isoniazid. *Mycobacterium phlei* and *Myco. smegmatis* metabolized citrate, cetoglutarate and malate but not oxalo-acetate, leucine or isoleucine.

These studies therefore reveal both quantitative and

qualitative metabolic differences between these virulent and avirulent mycobacteria and these differences would seem to be related to differences in ribonucleic acid content as isoniazid-resistant strains have been shown to contain less of this nucleic acid than do the sensitive strains (PAUNESCO and GEORGESCO, *Probl. Terap.*, 1959, v. 10, 131). The results of previous studies [this *Bulletin*, 1959, v. 34, 279] also indicate that the changes in the metabolism of acetate and its precursors may be related to the deficiency of the cytotoxic lipids of the avirulent strains. S. R. M. Bushby

OTT, J. L. Asparaginase from *Mycobacteria*. *J. Bacteriology*. 1960, Sept., v. 80, No. 3, 355-61, 5 figs. [11 refs.]

BOISVERT, H. L'identification des mycobactéries par la recherche de l'acide nicotinique. [Identification of *Mycobacteria* by the Demonstration of Nicotinic Acid] *Ann. Inst. Pasteur.* 1960, Oct., v. 99, No. 4, 600-607. [27 refs.]

The English summary appended to the paper is as follows:—

"Konno's reaction is carried out on cultures on Jensen's medium, seeded at three points, and kept a month in the incubator. Bovine smooth dysgonic strains are cultivated on pyruvate medium.

"From 168 human strains, 162 are positive; 5 are dubious; 1 is negative (H37RvD).

"From 26 bovine strains, two are dubious, 2 collection strains are positive.

"One strain of BCG out of 12 (Moscou) is positive; 3 strains of Wells bacillus are positive; 1 strain of *M. ulcerans* is dubious; 16 avian strains, 1 *M. balnei* and 2 *M. fortuitum* are negative.

"From 74 paratuberculous strains (3 of which are photochromogeneous) 1 is dubious, the other ones are negative.

"Eight *Nocardia* and one *Corynebacterium* are negative.

"Konno's reaction is very simple and should be used in routine laboratory practice. However, it must be cautiously interpreted, and the nature of the medium, the age and the abundance of the culture must always be kept in mind."

BJERKEDAL, T. Acquisition of Resistance in Guinea Pigs infected with Different Doses of Virulent Tubercle Bacilli. *Amer. J. Hyg.* 1960, July, v. 72, No. 1, 130-48, 7 figs. [10 refs.]

This paper is a continuation of the analysis of the results of 2 experiments in which 467 and 947 guineapigs, respectively, were used; for the first reports see [this *Bulletin*, 1960, v. 35, 1035]. In each of these experiments the animals had been divided into 6 groups, and inoculated with H37Rv in decreasing doses from approximately 10^6 to 10^1 . The animals had been observed for 2 years and post-mortem examinations were made on those that died and those that survived this period.

In this paper the results are analysed from several aspects and extensively discussed. Comparison between the number of bacilli in the infecting dose and the survival time of the animals indicates that the lesions at the time of death are the same irrespective of the dose, but that the survival time becomes progressively longer as the dose is successively decreased by 10-fold reductions, and that differences in virulence of the infecting bacilli only change the quantitative aspect of the relation between initial numbers of infecting bacilli and survival time.

These results are interpreted as showing that the resistance an animal acquires in response to the infection depends primarily on the host characteristics and is in the main independent of the size of the infecting dose. Resistance is apparently established within a few weeks and its effect on the inhibitory multiplication of the bacilli is related inversely to the number of bacilli to be acted on at any given time. The course of the infection therefore depends on the degree of resistance an animal establishes and the number of bacilli present at the time the resistance becomes fully developed.

S. R. M. Bushby

YOUATT, Jean. **The Metabolism of Isoniazid and other Hydrazides by Mycobacteria.** *Australian J. Exper. Biol. & Med. Sci.* 1960, June, v. 38, Pt. 3, 245-50, 3 figs.

Hydrazides were added to suspensions of isoniazid-sensitive and isoniazid-resistant BCG in phosphate buffer pH 7 and were shaken in air. At intervals of up to 24 or 48 hours samples were removed for estimations of the hydrazides and, where possible, of the corresponding acid. Heat-killed suspensions were used as controls.

The results showed that BCG, irrespective of its sensitivity to isoniazid, metabolized isoniazid and the hydrazides of nicotinic acid, benzoic acid and picolinic acid. Because not only is the presence of oxygen essential but also because the changes are inhibited by the presence of sodium cyanide and sodium azide, the process is considered to be a direct action and to be analogous to a detoxication rather than to being related to the mode of action of the antituberculous activity of isoniazid. Killed tubercle bacilli were also shown to break down isoniazid but this was attributed to a chemical action perhaps similar to that which occurs in the presence of haemin.

From the results of experiments with radioactive isoniazid which are to be reported elsewhere it appears that resistant strains metabolize isoniazid as fast as they take it up, whereas sensitive strains bind isoniazid more rapidly than they can metabolize it. [For previous studies by the author, see this *Bulletin*, 1959, v. 34, 379, 380.]

S. R. M. Bushby

"Other hydrazides inhibited the uptake of isoniazid. If the hydrazide group was substituted there was no inhibition. C¹⁴ nicotinic acid hydrazide was taken up at approximately one-third of the rate of uptake of isoniazid. The uptake required oxygen and was sensitive to sodium cyanide and azide. In this the uptake resembled that of isoniazid, but there was no inhibition by other hydrazides even in large excess.

"Hydrazones of isoniazid were taken up by a different process which did not require oxygen and was insensitive to cyanide.

"These results are discussed in terms of the mode of action of isoniazid."

SUBBAIAH, T. V., MITCHISON, D. A. & SELKON, J. B. **The Susceptibility to Hydrogen Peroxide of Indian and British Isoniazid-Sensitive and Isoniazid-Resistant Tubercle Bacilli.** *Tubercle*. 1960, Oct., v. 41, No. 5, 323-33, 1 fig. [19 refs.]

KREIS and LE JOUBIUX [this *Bulletin*, 1957, v. 32, 803] described a quantitative test for measuring the sensitivity of tubercle bacilli to the lethal effects of hydrogen peroxide but it proved unsuitable for determining the sensitivity of a mixture in which the resistant organisms were present in low proportion. By reducing the concentrations of hydrogen peroxide to 0.02% and the exposure time to 90 minutes at 37°C. the present authors claim to have made the test suitable for mixed cultures.

By using this modified method 8 strains of isoniazid-sensitive bacilli from British patients were found to be resistant to the peroxide, whereas of 7 similar strains from Indian patients 4 were decidedly more peroxide-sensitive than the British strains. Of 7 British strains that were isoniazid-resistant but had retained some catalase activity, all contained at least 0.11% peroxide-resistant bacilli, and, in contrast, 3 of the 8 isoniazid-resistant, catalase-positive strains from Indian patients contained 0.018% or less peroxide-resistant organisms. All of the 9 catalase-negative, isoniazid-resistant strains from both British and Indian patients were completely susceptible to the peroxide.

An association was found between low catalase activity, high susceptibility to peroxide and a high degree of resistance to isoniazid, especially among the British strains. The relationship between peroxide susceptibility and animal virulence of the Indian strains is being investigated.

An incidental observation made during the study was that a variant of H37Rv selected in 1953 and found then to be resistant to 50 µgm. isoniazid per ml. and catalase-negative, was now found to contain reverse-mutants which were resistant to the peroxide and catalase-positive.

S. R. M. Bushby

YOUATT, Jean. **The Uptake of Isoniazid and Related Compounds by Mycobacteria.** *Australian J. Exper. Biol. & Med. Sci.* 1960, Aug., v. 38, Pt. 4, 331-7, 1 fig.

TIRUNARAYANAN, M. O., VISCHER, W. A. & BRUHIN, H. **Some Properties of Catechol Peroxidase of Mycobacteria bearing on Isoniazid Susceptibility.** *J. Bacteriol.* 1960, Oct., v. 80, No. 4, 423-9, 1 fig. [15 refs.]

GRUMBACH, Françoise, with the technical collaboration of Sabine CLAVEL. *Activité antituberculeuse expérimentale de deux dérivés de phénazine pigmentée (B 663 et B 720) seuls et associés à d'autres antituberculeux (isoniazide et éthionamide). [Experimental Anti-Tuberculous Activity of Two Pigmented Phenazine Derivatives (B 663 and B 720), alone or associated with other Anti-Tuberculous Drugs (Isoniazid and Ethionamide)]* *Ann. Inst. Pasteur.* 1960, Oct., v. 99, No. 4, 567-85, 1 fig. [16 refs.]

These Rimino compounds, B663 and B720, have been extensively studied by BARRY and co-workers [this *Bulletin*, 1957, v. 32, 945] and the experiments described in the present paper confirm their findings.

In Youman's medium, the compounds inhibited the growth of H37Rv at 0.3-0.6 μ gm./ml., and in oral doses of 5-10 mgm./kgm. daily they gave similar protection to mice infected intravenously with H37Rv, when the treatment was started on the day of infection; but when the treatment was delayed for 14 days, B663 was very much more active than B720. In the first of these experiments the effect of treatment was judged by the extent of the disease after 22 days of treatment when 4 of the 6 control mice, but none of the treated animals, were dead and, judged by the extent of the disease, the protection appeared to be superior to that given by 1.25 mgm. isoniazid per kgm. The effect of the treatment in the second experiment, in which the treatment was delayed, was judged by the number of bacilli recoverable by culture from the lungs; doses of 25 mgm. and 50 mgm./kgm. gave protection similar to 5 mgm. isoniazid per kgm. or 50 mgm. ethionamide (1314 Th) per kgm., for after 30 days' treatment there was a marked fall in recoverable bacilli, but during the 30th to 60th day of treatment the number became stationary and resistant organisms were recoverable. When B663 was given in combination with isoniazid or ethionamide the reduction in the number of bacilli after the 30th day continued until only a very few bacilli were recoverable and no resistance developed. When treatment was stopped after 50 days, there was no multiplication of the bacilli even 48 days later and this was presumably due to retention of B663 in the tissues.

Both drugs are very non-toxic to mice for they tolerate a single dose of 2.5 gm./kgm. or daily doses of 50 mgm./kgm. for 3 months without harmful effect, and judging from the colour of the viscera the drugs accumulate and are retained in the tissues for long periods.

The author recommends that B663 be tried in man.

S. R. M. Bushby

MOUREAU, M. H., BRETEY, J. & ROY, D. *Thermo-résistance des mycobactéries tuberculeuses. Relation avec le pouvoir pathogène. Souches humaines, bovines, BCG, aviaires, paratuberculeuses. [Thermo-Resistance of Mycobacterium tuberculosis. Relationship with Pathogenicity (Human, Bovine, Avian, BCG and Paratuberculosis Strains)]* *Ann. Inst. Pasteur.* 1960, Sept. & Oct., v. 99, Nos. 3 & 4, 420-32; 586-99.

The English summary appended to the paper is as follows:—

"Experiments on the thermo-resistance of *M. tuberculosis* suspended in water and in milk (1 mg/ml) yielded the following results.

"The 10 human strains studied resisted to 70° during 15 minutes, 3 strains to 80° and 2 strains to 85°. The findings in water and in milk were similar.

"The 10 bovine strains studied resisted 10 minutes to 70°, 4 strains to 80° during 5 minutes, and 3 strains to 85° during 5 minutes. No resistance was observed at 90°.

"The avian strains yielded similar results, but the resistance of *M. paratuberculosis* strains was higher, often reaching 90°; but only a few colonies showed such a high thermo-resistance; with the dilution of the suspension, their number considerably decreased. It is probable that other authors who reported the existence of human or bovine *M. tuberculosis* strains resistant to 90° actually worked with *M. paratuberculosis*.

"All the details of the technique are described in the paper.

"In the second part, the authors describe their efforts to find out whether thermo-resistance acted by selecting pathogenic bacilli, or if it was due to pre-existing heat-resistant colonies. They did not succeed in stating any influence of heat on the pathogenicity of bacilli."

PANISSET, M., BENOIT, J. C., FRAPPIER, A. & SAINT-PIERRE, J. *Survie et multiplication du BCG et du bacille tuberculeux chez la souris. II. Comparaison de vaccins BCG lyophilisés préparés à partir de cultures de trois ages différents. [Survival and Multiplication of BCG and Tubercle Bacilli in Mice. II. Comparison of Freeze-Dried BCG Vaccines Made from Cultures of Three Different Ages]* *Ann. Inst. Pasteur.* 1960, Oct., v. 99, No. 4, 496-503.

The English summary appended to the paper is as follows:—

"The authors show that freeze-dried BCG vaccines, prepared with 7, 14 and 21 days old cultures, possess a protective capacity inversely proportional to the age of the culture in the vaccination against experimental tuberculosis in mice.

"They used their personal method: evaluation of the survival and multiplication of the superinfecting bacilli in the spleen."

FITZPATRICK, Florence K. *Effect of Cortisone on Mice infected with Chromogens and with Isoniazid Resistant Tubercle Bacilli. Proc. Soc. Exper. Biol. & Med.* 1960, Aug.-Sept., v. 104, No. 4, 558-60.

In preliminary experiments with H37Rv, 0.5 mgm. cortisone acetate administered subcutaneously for 7 days after infection was shown to be the minimum quantity of the drug that would significantly accelerate the death of mice infected intravenously. This dose of the steroid was then administered to mice infected with an isoniazid-resistant variant of H37Rv and it decreased the

survival time of 50% of the mice in 2 experiments from over 108 and over 110 days to 47 and 41 days respectively; in mice infected with 9 strains of photochromogens, 4 strains of scotochromogens and 7 strains of non-photochromogens (Battey type), the treatment had a similar virulence-enhancing effect in 3 of the photochromogens and 2 of the scotochromogens. The increased virulence was shown not only by an increase in mortality but in the number of acid-fast bacilli in the tissues and in the size of the lesions.

Although this dose of cortisone is far in excess of that usually used clinically, the author suggests that the effects seen in the mice might find their parallel in human infections under conditions of prolonged stress or anxiety.

S. R. M. Bushby

BÖNICKE, R. The Classification of Atypical Mycobacteria by their Power to Metabolize Amides. *German Med. Monthly.* 1960, July, v. 5, No. 7, 232-5, 2 figs. [Translation from *Tuberkulosearzt.* 1960, v. 14, 209.]

Equal volumes of an 0.00164 M solution of the amides and suspensions of the mycobacteria in M/15 phosphate buffer pH 7.2 were incubated at 37°C. for 2-3 hours and metabolism of the amide was detected by the liberation of ammonia, using the phenol hypochlorite method of Russell. The bacilli were derived from Löwenstein-Jensen slopes and were suspended in buffer to give a strength of approximately 10 mgm./ml. The results obtained were:

Mycobacterium	No. of strains tested	Amide							
		Acetamide	Benzamide	Urea	Iso-nicotinamide	Nicotinamide	Pyrazinamide	Salicylamide	Allantoin
<i>Myco. smegmatis</i>	12	(±)	+	+	+	+	+	(±)	-
<i>Myco. phlei</i>	12	-	-	+	-	+	+	-	-
<i>Myco. fortuitum</i>	10	+	-	+	-	-	-	-	+
Photochromogens									
—Runyon Group I	12	-	-	+	-	+	-	-	-
<i>Myco. avium</i>	12	-	-	-	-	+	+	-	-
Non-photochromogens									
—Runyon Group III	12	-	-	-	-	+	+	-	-

(±) weak production by 1 or 2 strains

These results show the value of the method for classifying mycobacteria, and the identical results obtained with the strains of *Myco. avium* and the Runyon Group III atypical mycobacteria support the contention that the bacilli are related.

S. R. M. Bushby

ROYAL NETHERLANDS TUBERCULOSIS ASS. The Occurrence of Atypical Mycobacterial Infections in the Netherlands and the Behaviour of the Bacteria in vitro [MANTEN, A.] *Proc. Tuberculosis Res. Counc.* 1959, No. 46, 71-82, 1 fig. [29 refs.]

Of the 66 strains sent as atypical mycobacteria to the author from various places in Holland and Belgium, 21 were classified as Runyon Group I (photochromogens), 5 as Runyon Group II (scotochromogens), 4 as Runyon Group III (non-photochromogens), and 2 as Runyon Group IV ("rapid growers"). Of the remaining strains, 4 proved to be tubercle bacilli, 12 to be saprophytes and the others were probably non-pathogens although they were not identified with certainty. The photochromogens, which the author classifies as *Mycobacterium luciflavum*, and the non-photochromogens were all from adult males, except possibly for 2 which were from patients whose age and sex were unknown; the scotochromogens, classified as *Myco. scrofulaceum*, were from 5 children.

The author considers the drug-sensitivity patterns of the strains to be of value in their classification. The photochromogenic strains were moderately resistant to isoniazid and to PAS, moderately sensitive to thiosemicarbazone and sensitive to thioamide. The scotochromogens were relatively sensitive to streptomycin and thiosemicarbazone, resistant to PAS and thioamide and highly resistant to isoniazid. The non-photochromogens and the rapid growers were resistant to all the drugs.

The author also briefly reviews the history and discusses the importance of the atypical mycobacteria.

S. R. M. Bushby

ROYAL NETHERLANDS TUBERCULOSIS ASS. The Behaviour of the So-Called Atypical Mycobacteria in the Animal Test [COSTER, J. F.]. *Proc. Tuberculosis Res. Counc.* 1959, No. 46, 83-8, 14 figs. on 7 pls. [15 refs.]

In this paper the author draws especial attention to the characteristic lesion produced by strains of *Mycobacterium luciflavum*, the yellow bacillus, in hamsters. [This species is presumably the Runyon Group I photochromogen.] The lesion, which develops at the intramuscular injection site, consists of mononuclear cells with oval-shaped or slightly bubble-shaped nuclei; it contains no giant cells but in places there are accumulations of lymphocytes and the lesion does not deteriorate. Miliary lesions develop in the viscera and these consist of cells similar to those of the granuloma of the injection site. Human and bovine strains of tubercle bacilli produce no progressive lesions and the strains of *Myco. scrofulaceum* or the "Battey" strains examined, either produced no lesion or doubtful epithelioid cell lesions in the liver and spleen.

S. R. M. Bushby

ROYAL NETHERLANDS TUBERCULOSIS ASS. "Atypical" Mycobacteria in Sanatorium Patients, hospitalized with the Diagnosis of Pulmonary Tuberculosis [OOSTERBAAN, I. N.] *Proc. Tuberculosis Res. Counc.* 1959, No 46, 89-107. [17 refs.]

This article begins with a review of some of the reports since 1918 of cases from which acid-fast bacilli

had been isolated and were apparently not tubercle bacilli, and of RUNYON'S classification of the "atypical" mycobacteria. The author then reports on 13 cases of his own from whom strains of photochromogens were isolated; they were 12 males and 1 female and were all over 20 years of age. None had lesions which were radiologically regarded as primary lesions and from none could the source of the infection be established. The lesions were usually in the right upper lobe.

All the strains were catalase positive and resistant to 1 or more μgm . isoniazid per ml., but 4 were sensitive to 10 μgm . streptomycin per ml. Each was isolated by culture and in guineapigs they produced no lesions. In 3 cases the organisms were also recovered from the resected lesions.

A non-photochromogen was also isolated from the sputum and resected specimen of a patient, but tubercle bacilli were grown from the sputum of this patient.

The incidence of adult cases diagnosed as tuberculosis and found to be exclusively excreting these organisms was about 1 in 50.

S. R. M. Bushby

ROYAL NETHERLANDS TUBERCULOSIS ASS. **The Use of Neutral Red in Culture Media for the Differentiation between *Mycobacterium tuberculosis* and Atypical Mycobacteria** [BEEUWKES, H.] *Proc. Tuberculosis Res. Counc.* 1959, No. 46, 108-12, 4 coloured figs. on 2 pls.

These observations were made on an egg-charcoal-agar medium, and on Löwenstein medium+charcoal and pyruvic acid, to both of which had been added approximately 15 mgm. neutral red per 100 ml.

After about 10 days' incubation tubercle bacilli grew on both media as strawberry coloured colonies but with a background coloured brown on the agar medium and greyish-green on the Löwenstein medium. Photochromogens produced violet discoloration of both media, due to a shift in pH, and even before exposure to light the colonies were yellowed. Although their colour deepened after exposure to light, the photochromogens would therefore appear to behave as scotochromogens in the presence of neutral red. Non-photochromogens produced the violet coloration of the media and their colonies were red.

S. R. M. Bushby

EDWARDS, D. C. **The Keto Acid Metabolism of *Corynebacterium diphtheriae* growing in Submerged Culture.** *J. General Microbiol.* 1960, Oct., v. 23, No. 2, 301-6, 4 figs. [13 refs.]

KATO, I. & PAPPENHEIMER, A. M., Jr. **An Early Effect of Diphtheria Toxin on the Metabolism of Mamalian Cells growing in Culture.** *J. Exper. Med.* 1960, Aug. 1, v. 112, No. 2, 329-49, 9 figs. [30 refs.]

An elaborate study of the effect of diphtheria toxin on the growth of cell cultures is presented. The strains used were HeLa tumour cells, the MK strain of human kidney cells and one derived from normal mouse spleen cells.

By means of the incorporation of radioactive forms of S, K and P in the culture medium and subsequent determination of the amount of these elements present in the cell growth, an endeavour has been made to determine the relative rates of protein synthesis in control cultures and in parallel ones in which the cells have been subjected to the action of highly purified diphtheria toxin. The principal deductions made from these observations are that no immediate cessation of protein synthesis was observed when the assimilation of methionine labelled with S or of K was the criterion. This effect was first observed after an interval of more than an hour. On using radioactive P as indicated, a marked fall in the rate of synthesis of ribonucleic acid was observed but, as with protein, only after 60 minutes. Deoxyribonucleic synthesis was not shown to be affected even after 3 hours.

The only very rapid action of the toxin which was recorded was its effect on synthesis of adenosine triphosphate, 40% inhibition of this activity being observed within 5 minutes of the exposure of the cells to toxin and since it is inhibited by antitoxin it was presumed to be a specific toxic effect. It was only observed, however, in media containing glucose. The observed actions of toxins are manifested at concentrations of the order of 0.1 Lf/ml., i.e. 7.5 MLD, and with greater concentrations.

In view of the fact that the mouse is relatively refractory to diphtheria toxin, it is of special interest that even at concentrations of 5 Lf/ml. of diphtheria toxin no similar effects were observed in cell cultures of mouse tissue.

The effect of the antibiotic Antimycin A on tissue cell cultures resembled that of diphtheria toxin. Antimycin is believed to exert its action by interference with the respiratory activities controlled by cytochromes.

J. W. Mcleod

RADOLA, B. J. **Electrophoretic Studies on Extracellular Diphtheria Proteins.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 7, 281-6, 6 figs. [11 refs.]

— **Extracellular Diphtheria Glycoproteins.** *Ibid.*, 287-92, 11 figs. [12 refs.]

The proteins referred to in these two papers were isolated from culture filtrates of *Corynebacterium diphtheriae*.

TARTLER, G. & SCIGALLA, G. **Experimenteller Beitrag zur Steigerung des Immunisierungseffektes bei Diphtherieimpfstoffen durch Adsorption des Di-Toxoids an Aluminiumstearatgele. (Experimentelle Untersuchungen am Meerschweinchen.) [Experimental Observations on the Increased Antigenic Effect of Diphtheria Prophylactics containing Toxoid adsorbed on Aluminium Stearate Gel (Experimental Observations on Guinea-pigs)]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, July, v. 6, No. 7, 431-8, 3 figs. [15 refs.]

Experimental work is described on the relative value of the standard diphtheria prophylactics and one which the authors have prepared by incorporating freeze-dried formol toxoid in a gel of aluminium stearate.

Guineapigs were immunized with subcutaneous injection of 0.5 ml. of the prophylactics and their sera were subsequently tested for antitoxin-content, the rabbit being used according to Jensen's technique. The preparations in 2% and 4% aluminium stearate showed themselves markedly superior to the standard diphtheria-tetanus toxoid absorbed on aluminium hydrate which is issued by the Serum Institute, Berlin-Pankow, and also to a preparation of toxoid incorporated in 10% aluminium stearate.

The description of the preparation of the toxoid gel mixture is given in considerable detail. *J. W. McLeod*

HOLLOWAY, B. W., EGAN, J. B. & MONK, Marilyn. **Lysogeny in *Pseudomonas aeruginosa*. Australian J. Exper. Biol. & Med. Sci.** 1960, Aug., v. 38, Pt. 4, 321-9, 2 figs. [20 refs.]

"An investigation has been made into lysogenicity and pyocinogenicity in *Pseudomonas aeruginosa*. The bacteriophages isolated were classified into groups on their antigenic properties and attempts have been made to correlate biological characteristics with this grouping. Multiple lysogeny in some strains is described, including one strain lysogenic for four unrelated phages.

"Certain of the bacterial strains are lysogenic for a phage having characteristics more typical of a virulent than of a temperate bacteriophage and the relationship of such strains to the isolation of virulent phages from natural sources is discussed.

"Reference is made to the application of this knowledge of *Pseudomonas* phages to genetic and epidemiological studies with this bacterium."

DETURK, W. E. & BERNHEIM, F. **The Inhibition of Enzyme Induction and Ammonia Assimilation in *Pseudomonas aeruginosa* by Sulfhydryl Compounds and by Cobalt, and its Reversal by Iron.** *Arch. Biochemistry.* 1960, Oct., v. 90, No. 2, 218-23, 2 figs.

GERICHTER, C. B. **The Dissemination of *Salmonella typhi*, *S. paratyphi A* and *S. paratyphi B* through the Organs of the White Mouse by Oral Infection.** *J. Hygiene.* 1960, Sept., v. 58, No. 3, 307-19.

When typhoid or paratyphoid bacilli were introduced into the stomach of the mouse by means of a fine nylon tube, attached to a syringe, passed through the mouth, the organisms appeared in the blood stream within a very short interval of time (the author's estimate being about half a minute) and a little later they could be detected in the liver, spleen, kidneys and lungs. With an infecting dose of 5×10^9 , the concentration in the blood 2-3 minutes after this dose had been given was about 5×10^2 organisms per ml. The count increased from this and reached a peak of about 3×10^3 after some 20 minutes, when it began to fall. At the end of 3 hours it had fallen to 1.7×10^2 , but it was several days before the blood was sterile. The very rapid appearance of the organism in the blood stream after oral administration

is a matter of considerable interest. Most workers have been of the opinion that the organisms pass from the intestine to the blood via the mesenteric glands, lymph channels and thoracic duct, whereas the author favours the view that they pass directly into the blood stream by way of the intestinal capillaries. It certainly seems more reasonable, in view of the relatively long journey by way of the lymphatic system and the fact that the organisms reach the blood stream within 20-30 seconds, to accept the shorter route; the villi of the small intestine are rich in capillaries so that there is a large absorptive area.

The essential differences in the results obtained by the oral administration as compared with intraperitoneal injection appear to be primarily related to the very wide differences in the degree of invasion of the blood stream by the organisms from the site of inoculation; from the intestine relatively few organisms invade the blood stream but from the peritoneum a very high proportion of the bacteria inoculated pass rapidly into the blood. Within 2-3 minutes of injecting 5×10^7 typhoid bacilli into the peritoneum of a mouse, 5×10^3 bacilli per ml. were found in the blood; within the same interval with the oral administration of a dose 100 times greater than the intraperitoneal dose there were 10 times fewer organisms in 1 ml. of blood.

These quantitative experiments with organisms, which do not multiply in the mouse, are full of interest and the original paper should be consulted for only a few points can be indicated in this abstract. *H. J. Bensted*

BILLAUELLE, H. **Studien an *Salmonella typhi*. 2. Immunologische und toxikologische Untersuchungen mit Extrakten und Fraktionen aus *S. typhi*. [Studies on *Salmonella typhi*. 2. Immunological and Toxicological Investigations with Extracts and Fractions of *Salmonella typhi*]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, July, v. 120, No. 1, 6-21, 15 figs. [22 refs.]

In the first paper of this series [this *Bulletin*, 1960, v. 35, 923] the preparation of various antigenic extracts and fractions of *Salmonella typhi* was described. The effectiveness of these different fractions in immunizing mice is discussed in this paper. Those studied were: (i) a water-soluble freeze-thawed extract (Fraction A); (ii) an ethanol or acetone purified glycoprotein-lipoid complex (Fraction B); (iii) the supernatant of (ii), containing nucleotides and free organic acids (Fraction C); and (iv) the bacterial stromata (Fraction D). Single doses of 1-100 μ gm. fraction A, 1-50 μ gm. fraction B or 10-100 μ gm. fraction C gave good protection in mice against infection with the parent strain of *Salm. typhi*, both immunizing and challenge doses being administered by the peritoneal route. These fractions remained immunogenically active for 6 years if kept in evacuated ampoules at 4-6°C. The stromal fraction was relatively ineffective, although a dose of 100 μ gm. conferred some protection.

Fractions B and D were the most pyrogenic in rabbits, fraction A less so and fraction C remarkably non-pyrogenic given its considerable effectiveness as an antigen. A dose of 5,000 μ gm. of fraction C per kgm. body

weight was required to produce a comparable pyrogenic effect in rabbits to 0.5 μ gm. of fraction B and 1 μ gm. of fraction D. The relationship of fractions B and C remains uncertain, i.e. whether they possess the same immunogenic material, whether the difference in their respective pyrogenic activities is a qualitative or quantitative one, and whether the immunogenic activity of fraction C is conceivably a matter of sensitization of the mouse's peritoneal cavity and not of an immune reaction.

B. Moore

BARON, L. S., SPILMAN, W. M. & CAREY, W. F. **Diploid Heterozygous Hybrids from Matings between *Escherichia coli* and *Salmonella typhosa*.** *J. Exper. Med.* 1960, Aug. 1, v. 112, No. 2, 361-72, 1 text fig. & 2 figs. on pl. [24 refs.]

This paper is concerned with an analysis of hybrids from crosses between *Escherichia coli* and *Salmonella typhi*, in which the *Salm. typhi* strains behave as recipient (female) organisms for genetic material transferred from the *E. coli* (male) cells.

A high frequency of recombination derivative of *E. coli* K-12, Hfr strain W-1895, was used for this work, and for the detection of strains fertile with this culture the various cultures of *Salm. typhi* which were to be tested as recipients were spread with the *E. coli* culture as the donor strain at a ratio of 20 recipient cells to 1 donor cell on an appropriate selective medium. The Hfr strain of *E. coli* K-12 was shown to mate at low frequency with several strains of *Salm. typhi*. The hybrids, which were selected as lactose positive, retained all the other biochemical and antigenic characteristics of *Salm. typhi*. One of these hybrids was remated with the Hfr *coli* strain and plated on minimal media having L-rhamnose, D-xylose, L-arabinose or L-fucose as the sole carbon sources. Hybrids of the remated strain appeared on the L-arabinose plates at high frequency and could be detected at lower frequencies on plates of the other media. Those selected for D-xylose or L-rhamnose utilization had the characters of segregating diploid heterozygotes; they were highly unstable and continually segregating a cultural form typical of the typhoid parent. The unstable type had most of the biochemical characters of the *E. coli* parent including the ability to produce indole and reacted to both *E. coli* and *Salm. typhi* antisera. One of the hybrid types had acquired susceptibility to several of the T phages, a characteristic of the *E. coli* parent, and a reduction in the mouse-virulence was found with the diploid hybrid form of *Salm. typhi*.

H. J. Bensted

RISCHE, H. & SCHNEIDER, H. Ergebnisse der Lysotypie von *Salmonella paratyphi B* unter besonderer Berücksichtigung der "Natürlichen Gruppierung" von Scholtens. [Results of Lysotyping of *Salm. paratyphi B* in Relation to the "Natural Grouping" of Scholtens] *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 1, 32-53. [17 refs.]

VLĂDOIANU, I. R., RUSSU, V. V., NAȘ, Lîgia & STREJNICU, F. Recherches expérimentales concernant la méthode mixte (orale-sous-cutanée) de la vaccination anti-typhoïdique. [Experimental Investigations concerning the Combined (Oral-Subcutaneous) Method of Typhoid Vaccination] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Mar., v. 19, No. 1, 137-47. [14 refs.]

The authors found that immunization of mice against *Salmonella typhi-murium* with 3 doses of vaccine given orally at 48-hour intervals, followed by 1 dose given subcutaneously 20 days after the last oral dose, resulted in better protection against the subsequent challenge than when the immunization was carried out by the subcutaneous route throughout. When they used a similar method for the vaccination of man with TAB vaccine they concluded that the results, based on the agglutinin response, indicated that combined oral and subcutaneous methods of inoculation gave a higher degree of protection than the usual simple subcutaneous injections.

[See this Bulletin, 1959, v. 34, 613, 1237.]

H. J. Bensted

COLLARD, P. & SEN, R. Serotypes of *Salmonella* at Ibadan, Nigeria, with special note of the New Serotypes isolated in Nigeria. *J. Infect. Dis.* 1960, May-June, v. 106, No. 3, 270-75. [16 refs.]

This is a record of the salmonella serotypes isolated during the 3 years 1956-58 in the Department of Bacteriology of University College, Ibadan. There were 131 different serotypes of which 44 had not been described previously; 12 of the new types were isolated from non-human material. The types are listed in detail, with their sources.

H. J. Bensted

ZWART, P. *Salmonella* and Arizona Infections in Reptiles in Netherlands. *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 3, 250-54. [18 refs.]

"A survey is given of *Arizona* and *Salmonella* types isolated from reptiles in Dutch zoological gardens.

"The importance of these findings with respect to public health are discussed."

GLANVILLE, E. V. & DEMEREC, M. Threonine, Isoleucine, and Isoleucine-Valine Mutants of *Salmonella typhimurium*. *Genetics.* 1960, Oct., v. 45, No. 10, 1359-74, 3 figs. [20 refs.]

WAGNER, R. P. & BERGQUIST, Arloa. Nature of the Genetic Blocks in the Isoleucine-Valine Mutants of *Salmonella*. *Genetics.* 1960, Oct., v. 45, No. 10, 1375-86, 6 figs. [23 refs.]

DIXON, J. M. S. & CURTIS, Betty A. **A Sucrose-Fermenting Strain of *Salmonella* Poona.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service* (directed by Med. Res. Council). 1960, Oct., v. 19, 193-4.

"A sucrose-fermenting strain of *S. poona* that was isolated from a poultry-packing establishment is described."

LE MINOR, L., RAVISSE, P. & DRÉAN, D. Un nouveau sérotype de *Salmonella*: *S. Mpila* (3,10:z38:z42). [A New *Salmonella* Serotype: *Salm. Mpila* (3,10:z38:z42)]. *Bull. Soc. Path. Exot.* 1960, May-June, v. 53, No 3, 402-3.

MORTELMANS, J., CLAEYS, R. & GUINÉE, P. A. M. A New *Salmonella* Type (*S. ngozi*) isolated separately in its Monophasic and Biphasic Form from a Dog and a Gecko. *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 3, 255-6.

"A new *Salmonella* type, which was first isolated from a dog as a monophasic strain (48:z₁₀; -) and some months later from a gecko as a biphasic strain (48:z₁₀; 1.5) is described."

GUINÉE, P. A. M. & KAMPELMACHER, E. H. Two New *Salmonella* Types (*S. Rotterdam* and *S. Blijdorp*). *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No.3, 329-30.

"A description is given of two new *Salmonella* types *S. rotterdam* with antigenic formula 1, 13, 22: g, t: 1,5 was isolated from the feces of a tree-agame (*Colotes versicolor*). *S. blijdorp* with the antigenic formula 1, 6, 14, 25:c:1,5 was isolated from the feces of a chameleon (*Chameleon jacksoni*)."

BUCKLAND, F. E. **Detection of Bacterial Antigens by means of Sensitized Guinea-Pig Ileum.** *J. Hygiene.* 1960, Sept., v. 58, No. 3, 291-5. [11 refs.]

The object of the experiments recorded in this paper was to determine the smallest amount of a bacterial antigen that would cause a significant anaphylactic response in the isolated ileum of a guineapig which had been specifically sensitized by the intraperitoneal injection of the appropriate antiserum 48 hours before being killed for the test.

It was found that a specific sensitive reaction was obtained with as little as 1 µgm./ml. of disintegrated whole cultures of various bacteria. In the case of *Shigella dysenteriae* (Shiga's bacillus) and *Salmonella typhi-murium*, purified polysaccharide preparations were available and here the specific reaction was obtained with 0.01 µgm./ml. of the material. The degraded polysaccharide of the antigen of Shiga's bacillus could be

detected with consistency at the 1.0 µgm./ml. level, but lower concentrations gave irregular results.

H. J. Bensted

ISTRATI, G. Lysotypie des *Shigella*. Note I. Schéma provisoire de lysotypie de *Sh. flexneri* Type 2a à l'aide des spécimens de phages endogènes provenant des souches paracoli aérogènes et anaérogènes, adaptés à différentes souches d'entérobactériacées. [Lysotyping of *Shigellae*. I. Provisional Pattern for the Lysotyping of *Sh. flexneri* Type 2a by means of Endogenous Phages of the Paracoli Strain adapted to Various Enterobacteriaceae] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Mar., v. 19, No. 1, 85-94. [24 refs.]

Bacteriophages isolated from lysogenic strains of paracolon bacilli of faecal origin were found to be readily adaptable, whereas those obtained from strains isolated from raw water supplies, or even dysentery bacilli themselves, were not so adaptable. Four phages were isolated from 4 lysogenic strains of paracolon bacilli; these were adapted to smooth and rough strains of *Shigella flexneri* Type 2a, *Sh. boydii* and certain strains of paracolon bacilli and also *Escherichia coli* and 15 phage variants were obtained, in 14 of which the spectrum was different. When these were tested against a number of strains of *Sh. flexneri* isolated from sporadic cases of bacillary dysentery it was found possible to classify these strains provisionally, in accordance with the phage patterning into 11 lysotypes and 18 sub-types. The results, however, suggested that changes might occur during repeated subculture or prolonged storage in the laboratory, but it seemed that the method had a useful application and one which could possibly be extended to dysentery bacilli outside the Flexner group.

[See below.]

H. J. Bensted

ISTRATI, G. Lysotypie des souches des *Shigella flexneri* 2a provenant de quatre foyers de dysenterie. Note II. [Lysotyping of *Shigella flexneri* 2a Strains isolated from Four Foci of Dysentery. II] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Mar., v. 19, No. 1, 95-101.

75 strains of *Shigella flexneri* Type 2a, isolated from 4 different outbreaks and one from a laboratory infection, were phage tested with the 14 phage preparations reported in the first part of this article. It was found that the strains isolated from 3 of the outbreaks had different phage-patterns, but that all the strains derived from the same outbreak had the same pattern. With regard to the other outbreak the strains were found to belong to 2 different serological sub-types, but by the phage-typing technique there were 5 lysotypes. [While it would appear that the technique devised by the author has some value as an epidemiological tool, minor antigenic variation, which may occur in the laboratory with many Flexner strains, may also upset the phage-patterning and limit its application in epidemiology.]

[See above.]

H. J. Bensted

IGNATOVA, M. I. **Study of the Thermolabile Antigen of *Shigella flexneri* (Types C and F) and of its Antigenic Properties.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 9, 101-6. [10 refs.] [Translated from Russian.]

This paper describes the presence of a thermolabile antigen in cultures of Flexner dysentery bacilli. The antigen was present in the live culture and also in formalized suspensions but it was destroyed by heating at 120°C. for half an hour. Heating at 60°C. for half an hour reduced the activity of the antigen but it usually required autoclaving for its complete destruction. Rabbit antisera prepared by immunizing animals with either living or formalized suspensions of Flexner organisms, absorbed with autoclaved homologous suspensions would agglutinate only formalized or living suspensions whereas the original antiserum also agglutinated an autoclaved suspension. The absorbed serum agglutinated equally well the author's Flexner types C and f, indicating that the thermolabile antigen of the two types are either identical or very closely related, but all the strains tested did not appear to contain this antigen and in some the antigen was poorly developed according to the results obtained with the absorbed sera. The results obtained in a haemagglutination-inhibition test were of the same order. Some mouse protection tests were done to show that vaccines containing both the thermostable and the thermolabile antigens gave better protection than those containing only the thermostable antigen.

[The author's approach to this work appears to have been largely conditioned by KAUFFMANN'S descriptions of the K antigens and FELIX'S work on the Vi antigen. While it may be true that the antigen described in this paper is in fact a K-antigen the information made available is not sufficiently detailed to make this certain. Fimbrial antigens (HOUWINK and VAN IJERSON, *Biochim. et Biophys. Acta.*, 1950, v. 5, 10) are commonly found on Flexner bacilli under certain conditions of culture and their properties, which have been fully described by DUGUID and GILLIES [this *Bulletin*, 1956, v. 31, 861; 1958, v. 33, 264; 1959, v. 34, 672], are very similar to those of this thermolabile antigen, but in the absence of an electron-microphotograph of the bacilli showing the characteristic appendages it is difficult to establish their identity.]

H. J. Bensted

KOZ'MIN-SOKOLOV, B. N. **Distribution and Duration of Persistence of Dysentery Bacilli in the Bodies of Passively Immunized White Mice.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 12, 90-97. [Translated from Russian.]

Flexner bacilli injected intraperitoneally into mice appear in the blood and the internal organs within 30 minutes. With lethal doses of about 40×10^6 bacilli the number of organisms found in the blood, liver, spleen, kidneys and mesenteric glands steadily increases and reaches a maximum at about 24 hours, when the animals are moribund, but the numbers found in the blood are as a rule significantly less than those found in the organs. In groups of mice receiving 9-10 PD50

doses of Flexner specific antiserum 24 hours before being given this intraperitoneal challenge of 40×10^6 Flexner cells of the same type, it was found that although the march of events was similar it was of a much lower order and gradually tailed off so that the mice, instead of dying at 24 hours, recovered and by about the 5th day Flexner organisms were no longer found in the blood or organs. Mice receiving normal serum behaved very much in the same way as those receiving no serum.

The effect of the antiserum was much more marked when the challenge was reduced to a sublethal dose— 5×10^6 bacterial cells—and the complete elimination of the challenge occurred earlier.

[These experiments are of interest not because they have importance with regard to the immunology of bacillary dysentery, which seems to be very doubtful, but as an experiment which can be applied to other organisms which are not natural pathogens of mice. There was no evidence from the author's experiments that the Flexner organisms multiplied in the tissues of the mice any more than the typhoid bacillus multiplies under similar conditions GERICHTER (see p. 189). With a natural pathogen, such as *Salmonella typhi-murium*, the behaviour of the mouse is entirely different.]

H. J. Bensted

IDINA, M. S. **The Period of Survival in Faeces of Dysentery Bacilli.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 12, 103-7. [Translated from Russian.]

Samples of faeces in which the approximate number of shigella organisms, *Shigella flexneri* or *Sh. sonnei*, was known were divided into a number of portions and stored under different temperature conditions. At regular intervals specimens for quantitative determination of the viable shigellae were collected from each of the samples. The samples all came from patients with acute bacillary dysentery, but as would be expected the viable counts varied considerably. Nevertheless the results showed that the temperature of -12°C. was generally the most favourable for survival and 37°C. the least favourable. At -12°C. the initial counts were maintained for long periods and viable organisms were still present at the end of 2 months, whereas at incubator temperature there were practically no survivors after 6 days. At room temperature the results were very variable. The maximum survival periods at ordinary refrigerator temperatures were 61 days and at room temperature 28 days.

[The results recorded in this paper are of considerable interest in indicating the long periods during which the Flexner and Sonne dysentery bacilli may remain viable in samples of faeces passed by dysentery patients. SPICER'S exact experiments [this *Bulletin*, 1959, v. 34, 1165] on the survival of *Sh. sonnei* on cotton threads showed that under the most favourable conditions the isolated organism could survive for 7-10 days, but he was well aware that surrounded by its natural exudate survival might be very much prolonged.]

H. J. Bensted

KOVALEVA, N. I. & MEKHEDOV, L. N. **The Multiplication of *Shigella sonnei* in Synthetic Media in Conditions of Aeration.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 9, 142-7, 2 figs. [Translated from Russian.]

This paper describes the intensive consumption of nitrogen-containing substances by *Shigella sonnei* when grown in a relatively simple synthetic medium under conditions of continuous aeration as compared with the same organism grown under stationary conditions. Additions of glucose, ammonium citrate and sodium hydroxide (for adjustment of the pH) were necessary to enable growth to continue at the same high rate. Ammonium citrate as the main source of nitrogen was superior to ammonia.

H. J. Bensted

MORGUNOV, I. N., MAKSIMOVICH, N. A. & YAGUD, S. I. **The Experimental Search for a Model for Dysentery. II. The Application of the Principle of Summation of Stimuli as a Pathogenic Mechanism to induce Dysentery in Cats.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 9, 92-101, 4 figs. [Translated from Russian.]

In a previous paper [see this *Bulletin*, 1960, v. 35, 1237] these authors describe the development of dysentery in cats by feeding cultures of *Shigella sonnei* to animals previously sensitized by the subcutaneous injection of toxin or endotoxin of dysentery bacilli. In the present paper they describe similar results when cats are fed with daily minimal doses of *Sh. sonnei*. They consider that the daily doses for the first few days produced the endotoxic effect by summation and that the further effects—rising temperature, leucocytosis, inflammatory lesions in the intestinal wall and the signs of dysentery, depended for their development on the toxic effect produced by the summation of the stimuli resulting from the daily minimal oral doses of dysentery cultures. If the total dosage spread over the period of the cultures fed were given in a single dose no infectious condition developed.

The authors feel the infective process in man might well be similar and that dysentery does not result from a single oral infection but from numerous repeated sub-infective doses.

H. J. Bensted

KAUFFMANN, F., BRAUN, O. H., LÜDERITZ, O., STIERLIN, H. & WESTPHAL, O. **Zur Immunchemie der O-Antigene von Enterobacteriaceae. IV. Analyse der Zuckerbausteine von *Escherichia*-O-Antigenen. [Immunochemistry of the O-Antigens of the Enterobacteriaceae]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 2, 180-88. [18 refs.]

The English summary appended to the paper is as follows:—

“The O antigens of 29 serologically classified *Escherichia coli* strains were isolated in the form of the purified lipopolysaccharides, the sugar constituents of which were determined. The analyzed O antigens belong

to 14 different chemotypes (I-IV, VI-VIII, X-XIII, and XVII-XIX).

“The following sugars were found to be constituents of *Escherichia* O antigens: galactosamine, glucosamine, heptose(s), galactose, glucose, mannose, fucose, rhamnose, and colitose (3-deoxy-L-fucose). Besides the most simple chemotypes with 4 sugars only (glucosamine, heptose, galactose/or mannose, and glucose) *E. coli* O antigens may be composed of 5 or 6 sugars; one chemotype (XII) was found to represent the combination of 7 sugars.

“The O antigens of *Coli-enteritis* strains often contain fucose or colitose. In *E. coli* species of other pathological or non-pathological origin fucose was found only rarely, colitose was absent.

“2 chemotypes of *E. coli* (XVII and XIX) do not contain galactose.

“The 14 hitherto elaborated chemotypes of *E. coli* O antigens were compared with the known chemotypes of *Salmonella* O antigens.”

LEVINE, E. M. & SIMMONDS, Sofia. **Metabolite Uptake by Serine-Glycine Auxotrophs of *Escherichia coli*.** *J. Biol. Chem.* 1960, Oct., v. 235, No. 10, 2902-9, 6 figs. [16 refs.]

ORTEGA, M. V. & BROWN, G. M. **Precursors of Nicotinic Acid in *Escherichia coli*.** *J. Biol. Chem.* 1960, Oct., v. 235, No. 10, 2939-45. [19 refs.]

HALPERN, Y. S. & UMBARGER, H. E. **Conversion of Ammonia to Amino Groups in *Escherichia coli*.** *J. Bacteriology.* 1960, Sept., v. 80, No. 3, 285-8. [10 refs.]

REITHEL, F. J. & KIM, J. C. **Studies on the β -Galactosidase isolated from *Escherichia coli* ML 308. I. The Effect of Some Ions on Enzymic Activity.** *Arch. Biochemistry.* 1960, Oct., v. 90, No. 2, 271-7, 4 figs. [12 refs.]

SANTER, M., TELLER, D. C. & ANDREWS, W. **Environment-Induced Changes in the Base Ratios of Ribonucleic Acid of *Escherichia coli*.** *J. Molecular Biol.* London. 1960, Nov., v. 2, No. 5, 273-5. [21 refs.]

BROWN, G. L. & ZUBAY, G. **Physical Properties of the Soluble RNA of *Escherichia coli*.** *J. Molecular Biol.* London. 1960, Nov., v. 2, No. 5, 287-96, 3 figs. & 1 pl. [32 refs.]

GUTHRIE, G. D. & SINSHEIMER, R. L. **Infection of Protoplasts of *Escherichia coli* by Subviral Particles of Bacteriophage ϕ X174.** *J. Molecular Biol.* London. 1960, Nov., v. 2, No. 5, 297-305, 6 figs. [12 refs.]

- GREER, S. B. **Growth Inhibitors and their Antagonists as Mutagens and Antimutagens in *Escherichia coli*.** *J. General Microbiol.* 1958, June, v. 18, No. 3, 543-64, 1 fig. [44 refs.]
- BANIC, S. **Isolation of Lac⁺ Mutants from a Lac⁻ Strain of *Escherichia coli*, by the Replica Plating Technique.** *J. General Microbiol.* 1958, June, v. 18, No. 3, 586-90, 4 figs. on pl.
- ENGLISH, A. R. **Studies on Tetracycline-Resistant *Escherichia coli* Strains and a Growth-Requirement for l-Histidine.** *Proc. Soc. Exper. Biol. & Med.* 1960, Oct., v. 105, No. 1, 156-8.
- WEATHERWAX, R. S. & LANDMAN, O. E. **Ultraviolet Light-Induced Mutation and Deoxyribonucleic Acid Synthesis in *Escherichia coli*.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 528-35, 3 figs. [18 refs.]
- TAYLOR, A. L. & ADELBURG, E. A. **Linkage Analysis with Very High Frequency Males of *Escherichia coli*.** *Genetics.* 1960, Sept., v. 45, No. 9, 1233-43, 6 figs. [14 refs.]
- See also p. 110, CARLUCCI & PRAMER, **An Evaluation of Factors affecting the Survival of *Escherichia coli* in Sea Water.** Parts I, II, III and IV.
- STENZEL, W. **Die Sorbosespaltung als Kriterium in der Diagnostik pathogener Enterobacteriaceen. [The Splitting of Sorbose as Criterion in the Diagnosis of Pathogenic Enterobacteriaceae]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 1, 19-26. [12 refs.]
- The English summary appended to the paper is as follows:—
- "In contrast to the Ballerup-Bethesda and Paracolobactrum coliform-group the germs of the genus *Salmonella* do not split sorbose at all or only with delay.
- "The practical significance of the sorbose reaction, especially for the differential diagnosis between Ballerup-Bethesda and *Salmonella*, was demonstrated by means of comparative examinations. Its limitations are pointed out.
- "The sorbose is of no value for the separation of the genus *Shigella* from the immobile *Paracolobactrum* strains, but it may be utilized for biochemical typing within the *Shigella* group."
- WEIBULL, C. & BECKMAN, H. **Metabolism of Small Bodies isolated from a Stable *Proteus* L Form.** [Correspondence.] *Nature.* 1960, Oct. 29, v. 188, 428-9, 1 fig.
- NEIDHARDT, F. C. **Mutant of *Aerobacter aerogenes* lacking Glucose Repression.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 536-43, 2 figs. [18 refs.]
- BARBER, Cella, STAMATESCU-EUSTATZIU, Silvia, TULPAN, Gertrude & PETROVICI, A. **Studies on the Specific (Somatic) Polysaccharides of *Klebsiella*.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 3, 379-83, 1 text fig. & 5 figs. on 3 pls.
- SCHIERHOLZ, H. & KAUFMANN, R. **Experimente zur Virulenzbestimmung von Bangbakterien im Kleinterversuch. [Animal Experiments for Virulence Determination of *Brucella abortus*]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 4, 509-21, 2 figs.
- An elaborate experimental investigation of the possibility of determining the virulence of *Brucella abortus* strains is described. A collection of 28 strains of widely varying apparent virulence have been examined for their capacity to produce lesions in experimental animals and to promote antibody formation, and also to influence the general nutrition in the animal body.
- The general outcome of these investigations has been negative, neither the extent of the lesions developed nor the titre of agglutinins produced in the blood sera could be shown to correspond at all closely to the virulence of the strain and although the animals receiving virulent strains put on weight on the average more slowly than controls or animals injected with strains of low virulence, this test could only be used in very carefully standardized conditions of diet and maintenance. J. W. McLeod
- PARNAS, J., LYSIKOWSKA, L. & KUZIELA, T. **Über die Beziehungen zwischen der Empfindlichkeit gegen Antibiotika, der Virulenz und dem Stoffwechsel von *Brucella brucei*-Stämmen. [On the Relationship between the Sensitivity against Antibiotics, the Virulence and Metabolism of *Brucella brucei* Strains]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 1, 68-80, 7 figs.
- The English summary appended to the paper is as follows:—
- "a) By means of SZYBASKY's method, 12 strains of *Brucella brucei* were obtained that showed resistance against Streptomycin (10,000 gr.) and 15 strains that were resistant against Aureomycin (500-1,000 gr.). The resistant strains were controlled for 16 months. Those strains resistant to Streptomycin showed stability in this respect, while those resistant against Aureomycin showed instability.
- "b) The group of Streptomycin resistant strains showed on each of three comparisons with the same group of the original strains a biochemical change in the urease- and catalase-activity and in the formation of H₂S. The differences were in the greater activity of the two ferments, and in the greater production of H₂S. The latter, however, was present for only a short time. Special bacteriostatic and serological changes were not noted. The group of Aureomycin resistant strains showed similar changes.

"c) The strains of *Brucella*, which had reached a high degree of virulence, also showed a greater urease-activity when compared with the original strains. The catalase-activity differed."

PIRSCH, Gerda W., DAY, W. C. & POLLOK, N. L. **Dihydrostreptomycin Aerosol Therapy for *Pasteurella tularensis* Infected Guinea Pigs.** *J. Infect. Dis.* 1960, May-June, v. 106, No. 3, 231-6, 1 fig. [10 refs.]

Guineapigs can be infected with tularaemia by inhalation of the organism in doses of 5.5 MLD or less, but the organism cannot be recovered from the blood until about 7 hours later. If, however, the animals are given inhalations of dihydrostreptomycin in doses of 1.1 mgm. soon after the aerosol infection they do not develop the disease, but if this is delayed too long or if the infecting dose is greater than 5.5 MLD the protective effect of the antibiotic is much reduced. Animals infected by the intramuscular or subcutaneous route are not protected by dihydrostreptomycin aerosols since only traces of the antibiotic find their way into the blood stream from the respiratory passages. When the organisms of tularaemia are inhaled by the guineapig they appear to be trapped or held in the terminal bronchioles or the lung (the size of the disseminated particles would not be greater than 5 μ) where they remain, for a limited period, within reach of the action of the antibiotic aerosol which presumably penetrates the full distance to the lungs also. Since the protective effect of inhaled dihydrostreptomycin on the tularaemia organisms is limited to the period where they are lodged in the lung, and before there is any invasion of the blood stream, this form of therapy can only be successful if it is exhibited very soon after infection.

H. J. Bensted.

BRODIE, J. & HENDERSON, A. **A Case of Empyema Thoracis infected with *Pasteurella multocida*.** *Scottish Med. J.* Glasgow. 1960, Oct., v. 5, No. 10, 452-3. [17 refs.]

"A case of empyema thoracis is described, from which *Pasteurella multocida* was isolated on six occasions; the infection responded to 15 g. of sulphamerazine and 9 million units of penicillin."

DODIN, A. & BRYGOO, E. R. **Étude quantitative de l'utilisation des sucres par *Pasteurella pestis* souche E.V. en suspension non proliférantes. II. Le glucose. Autodestruction, à 37°, du pouvoir de dégrader le glucose pour les germes cultivés à 26°. [Quantitative Studies on Glucides Utilization by *Pasteurella pestis* Strain E.V., in Non-Proliferating Suspensions. II. Glucose. Disappearance at 37°C. of the Capacity to split Glucose by the Organisms cultivated at 26°C.]** *Ann. Inst. Pasteur.* 1960, May, v. 98, No. 5, 676-81, 2 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 193.]

DAVIES, D. G. **The Influence of Temperature and Humidity on Spore Formation and Germination in *Bacillus anthracis*.** *J. Hygiene.* 1960, v. 58, No. 2, 177-86. [18 refs.]

The effects of temperature and relative humidity on spore formation and spore germination have been studied in the search for an explanation of the greater persistence of anthrax infection in subtropical soils than in that of Great Britain. The technique of previous observations on the effect of relative humidity appeared to the author to have been inadequate.

That adopted was to dry thin layers of agar on microscope slides, completely, and then to expose these for 3 days in a series of closed jars in which the relative humidities were regulated from 20% to 100% by H_2SO_4 and water mixtures in the base of the jars. It was assumed that the agar would take up moisture in proportion to the humidity. After 3 days the slides were inoculated and observations on germination and spore-formation were made. It was determined that both spore-formation and germination were most rapid in optimum conditions for growth, i.e. about 37°C. in maximum humidity. Spore formation persisted even at low temperature and low humidities. Above 44°C. and below 20°C., however, germination did not occur nor did it occur at humidities less than 80%.

It is argued, therefore, that in British soil the spores incorporated with bone manures will persist in the winter but germinate in spring and summer when the vegetative forms will disappear owing to the activities of other soil micro-organisms, whereas in tropical and subtropical climates germination will, for the most part, be impeded by lack of moisture and unduly high temperatures and spores will persist as potential sources of infection.

J. W. McLeod

SLEIN, M. W. & LOGAN, G. F., Jr. **Mechanism of Action of the Toxin of *Bacillus anthracis*. I. Effect in vivo on some Blood Serum Components.** *J. Bacteriology.* 1960, July, v. 80, No. 1, 77-85, 1 fig. [29 refs.]

Both crude and purified toxin preparations were used and were derived from the avirulent Sterne strain of *Bacillus anthracis*. When these were injected intravenously into rabbits it was found that within 71 hours there was a moderate to marked increase in serum aldolase, phosphoglucose isomerase, glutamic oxaloacetic acid transaminase, amylase and cholesterol. If antiserum was injected at the same time as the toxin these changes were less marked. Unusual variations in serum glycoprotein were not noted.

Glucose and alkaline phosphatase increased markedly soon after the injection of the toxin. In contrast to the hyperglycaemia, which required both the protective antigen and the filter factor components of the toxin and which was prevented by antiserum, hyperphosphatasæmia could be produced by the protective antigen alone and was not prevented by antiserum. Hyperphosphatasæmia was produced when the filter factor was combined with the protective antigen, but not when only the filter factor was injected.

H. J. Bensted

BYCHENKO, B. D. & MATVEEV, K. I. **Certain Properties of *Clostridium perfringens* Type A, B, C, D, E and F in relation to the Typing of the Strains.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 12, 69-76. [16 refs.] [Translated from Russian.]

Two-hundred strains of *Cl. Welchii*, including 165 of Type A, 6 of B, 8 of C, 19 of D and 2 of F have been investigated. The principal points emphasized apart from the varied susceptibility of the toxins of one type to neutralization by the antitoxins produced for other types, are summarized in the second and third tables.

It is shown that only in Type A is there a close correspondence between lethal action and lecithinase activity: and only with D is there marked activation of the toxin by treatment with trypsin. Trypsin destroyed or greatly diminished the activity of the other toxins. Cultures of types B and F produced gas gangrene in experimental animals—mice, without the liquefaction of muscle whereas in infection with type A and C the two phenomena were associated.

Heat resistance of spores to 100°C. for one hour was observed with F strains and with some A strains but not with B, C and D strains. [There are a number of minor slips and misprints.] *J. W. McLeod*

TAMIMI, H. A., HILTBRAND, W. & LOERCHER, Helen. **Some Growth Requirements of *Bacteroides fragilis*.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 472-6. [19 refs.]

BHASKARAN, K. **Recombination of Characters between Mutant Stocks of *Vibrio cholerae*, Strain 162.** *J. General Microbiol.* 1960, Aug., v. 23, No. 1, 47-54. [12 refs.]

"Crosses between two mutant strains derived from *Vibrio cholerae*, one requiring valine and isoleucine and the other arginine and purine, yielded recombinants when seeded together on a minimal medium containing L-asparagine. Other markers such as resistance or sensitivity to streptomycin and a lytic cholera phage, which were unselected under the experimental conditions, also segregated in the recombinants."

ABOU-GAREEB, A. H. **Experimental Study of Cholera Vibrio Strains in Tank Waters.** *J. Trop. Med. & Hyg.* 1960, Aug., v. 63, No. 8, 192-4.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 195.]

POKORNÝ, J. & SOBĚSLAVSKÝ, O. **Pokus o izolaci leptospír z vodních ptáků.** [An Attempt to isolate Leptospirae from Water-Fowl] *Českoslov. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 7, 505-6.

The English summary appended to the paper is as follows:—

"The total of 110 individuals of water-fowl of nineteen species from a region in South Bohemia with many lakes were investigated by cultivation for leptospirae. All isolation trials from liver and spleen were negative."

ELLINGHAUSEN, H. C., Jr. **Some Observations on Cultural and Biochemical Characteristics of *Leptospira pomona*.** *J. Infect. Dis.* 1960, May-June, v. 106, No. 3, 237-44, 6 figs. [18 refs.]

A few studies of the nutritional characteristics of leptospirae have been published but they deal mainly with *Leptospira canicola* [this *Bulletin*, 1951, v. 26, 184; 1952, v. 27, 491] and *L. icterohaemorrhagiae* [ibid., 1956, v. 31, 865]. The importance of *L. pomona* as the principal cause of the leptospirosis in cattle and other livestock [particularly in the U.S.A.] prompted the author to study the variable factors which might influence the growth pattern of this serotype (strain Johnson) in culture. A nephelometric method of determining the rate of growth of the leptospirae was used (Ellinghausen, *Amer. J. Vet. Res.*, 1959, v. 20, 1072).

Four media were evaluated. Schüffner's and Korthof's media have three disadvantages: the phosphate constituents are liable to precipitate; they are tedious to compound; and they cannot readily be stored in concentrated stock solutions. With Chang's medium there is a lag period and a lower degree of total growth. Stuart's medium had none of these disadvantages. For the remainder of the investigations a modified Stuart's medium was used (*loc cit.*).

A comparison of distilled water, deionized distilled, and tap water as diluents for the Stuart's medium revealed little difference in growth-supporting capacity; but concentrates ($\times 20$) of the constituent salts made with tap water (pH 6.8) were less resistant to bacterial contamination than those made with the other waters (pH 4.4). In samples of medium containing 7% rabbit serum, omission of both the phosphate buffer salts resulted in slightly less growth; but when only one buffer was omitted, the more alkaline medium (pH 7.4) was better than the other (pH 6.7).

The concentration of serum in the medium affected the growth rate and total growth of *L. pomona*. With no serum there was little growth support. There was a progressive increase in growth rate and in total growth with serum levels of 2 to 12%; higher levels resulted in depression of total growths.

The nutritive value of sera varied among animal species (rabbit is the best) and among individual animals. Rabbit serum derived from large pools is therefore less liable to be of poor nutritive value.

There was very little fluctuation in pH and Eh values of the medium during the incubation period. An initial pH of 7.4 was optimal for growth of *L. pomona*.

The age and density of the inoculum affected the growth pattern: a lag occurred with inocula aged 15 days or more, and with those of lower density. The total

growth after 9–10 days, however, was about the same, regardless of the density of the inoculum.

The optimal temperature for total growth and maximal growth rate was 29°C. Cultivation at lower temperatures (25°C. or less) resulted in slower growth; higher temperatures (32–37°C.) caused a faster initial growth but, if maintained, damaged the leptospire and depressed the total growth.

L. H. Turner

JOHNSON, R. C. & WILSON, J. B. **Nutrition of *Leptospira pomona*.** *J. Bacteriology*. 1960, Sept., v. 80, No. 3, 406–11. [13 refs.]

WELSHIMER, H. J. **Survival of *Listeria monocytogenes* in Soil.** *J. Bacteriology*. 1960, Sept., v. 80, No. 3, 316–20, 4 figs.

BACTERIOPHAGES

TERASIMA, T. **Further Report of Radiobiological Studies on Phage Multiplication in Lysogenic Bacteria. Genetic Recombination Phenomenon occurring between Phage and its Host Cell.** *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 397–410, 6 figs. & 1 pl. [12 refs.]

These experiments were done with phage β , isolated from a lysogenic strain of *Escherichia coli* (strain A 34), and *Shigella flexneri* 5 (KA).

Complexes were found to show a sudden increase in sensitivity to UV light soon after infection with phage and it had been postulated that this was due to the establishment of new UV sensitive targets during the early stages of phage development. However, a sharp increase in sensitivity to increasing UV dose was also observed when phage and bacteria were irradiated separately before infection, and the greater the UV dose the cells received before infection with irradiated phage the greater the inactivation of the phage. It is therefore suggested that the increased sensitivity of the complexes does not depend upon the development of new targets but upon the destruction of cellular material which reactivates irradiated phage. Components are postulated to be common to both host and phage, some concerned in reactivation in the undamaged cell, some only in the UV irradiated cell.

Plaque type mutants were found to be more frequent among the progeny of phage grown in irradiated bacteria than that grown in unirradiated bacteria, whether or not

the phage particles themselves had been irradiated. This is considered to be further evidence that bacterial genetic material (in this case altered by irradiation) is substituted for phage material during reactivation. Genetic homology between host cell and phage has previously been proposed by GAREN and ZINDER (*Virology*, 1955, v. 1, 347) and TESSMAN [*ibid.*, 1956, v. 2, 679; this *Bulletin*, 1957, v. 32, (275)] among others. Janice Taverne

FLEISCHMAN, J. B. **The Physical Properties of DNA from T2 and T4 Bacteriophage.** *J. Molecular Biol.* London. 1960, Oct., v. 2, No. 4, 226–40, 9 figs. [40 refs.]

NOMURA, M., HALL, B. D. & SPIEGELMAN, S. **Characterization of RNA synthesized in *Escherichia coli* after Bacteriophage T2 Infection.** *J. Molecular Biol.* London. 1960, Nov., v. 2, No. 5, 306–24, 8 figs. and 1 pl. [22 refs.]

UCHIDA, H. & STENT, G. S. **Protein Synthesis and the Onset of Intracellular Bacteriophage Growth. I. Stabilization of the Infecting Phage to ^{32}P Decay.** *J. Molecular Biol.* London. 1960, Nov., v. 2, No. 5, 251–61, 4 figs. [38 refs.] **II. Stabilization to ^{32}P Decay of the Genome of a Secondary phage.** *Ibid.*, 262–72, 2 figs. [15 refs.]

VIRUSES

The order in this section is:—General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.

ANN. NEW YORK ACAD. SCI. 1959, July 21, v. 81, Art. 1, 1–213, numerous figs. [Numerous refs.] **The Cytopathology of Virus Infection** [LOVE, R. (Conference Chairman)]. [Conference held Nov. 7 and 8, 1958.]

This is a valuable collection of 20 papers on various aspects of a subject about which published information is very scattered. In the first paper (pp. 6–16) W. J. CHEATHAM discusses the correlation between the lesions

of varicella in tissue culture and the lesions in man: in both, the lesions are focal and spread is either between contiguous cells or by carriage of an infected cell from a focus to a new area. Herpes zoster appears to be confined to nervous tissue because it occurs in the presence of circulating antibody. In measles giant cells are formed both in tissue culture and in lymphoid and respiratory tissues of man. M. REISSIG (pp. 17–28) describes double infection of monkey kidney cells with measles

and poliovirus which grow together each producing nuclear and cytoplasmic inclusions. Poliovirus multiplication is unaffected in doubly infected cells and in measles-induced giant cells is much greater than in mononuclear cells. Measles virus multiplication is reduced in doubly infected cells.

Three papers on the chemistry of virus-infected cells follow. H. F. MAASSAB and W. W. ACKERMANN (pp. 29-37), using radioactive phosphorus, found that HeLa cells infected with poliovirus have increased loss of ^{32}P after 6 hours indicating loss of cellular integrity. During the first 6 hours there was a steady increase of cytoplasmic RNA and protein; infectivity appeared after 3 hours and rapidly increased. C. C. RANDALL, W. M. TODD and G. A. GENTRY (pp. 38-50) studied equine abortion virus in hamster liver and HeLa cells: the nuclei of infected cells increased in size with a marked increase in DNA and protein (but not RNA) content. The lipid content also increased and this was marked in fowl scalp and chorio-allantoic cells infected with fowlpox. H. B. LEVY and I. BRODSKY (pp. 51-61) using ^{32}P to study a mouse leukaemia virus showed a marked increase of RNA and lipid in the microsome and subparticulate fractions but not in the nuclei and mitochondria of infected cells.

Time-lapse motion studies by P. LEPINE, C. CHANY, B. DROZ and F. ROBBE-FOSSAT (pp. 62-72) of myxovirus infections showed that multi-nucleate cells formed in response to HA1 virus arise by fusion of cells. The cytoplasmic inclusions of CA virus contained a high concentration of sulphhydrated RNA-protein and these apparently "fall out" leaving a "Swiss-cheesecake" effect.

C. LEUCHTENBERGER, G. S. BOYER and J. J. STRAIN (pp. 73-83) studied infections by DNA-viruses (verruca vulgaris, adenovirus) of several types of human cell by microspectrophotometry finding abnormal cytological and cytochemical changes in DNA in the cell. J. S. F. NIVEN (pp. 84-88) used acridine orange as a fluorescent dye together with specific enzymes to distinguish RNA and DNA in cells: with pox viruses DNA was found in the cytoplasm; and altered RNA pattern in the cytoplasm followed infection with West Nile virus; with influenza virus RNA was found in the nucleus where DNA aggregates appeared after adenovirus infection. W. R. ADAMS and A. M. PRINCE (pp. 89-100) described the changes in Ehrlich ascites tumour cells following infection with chick-embryo-adapted Newcastle disease virus (NDV), as observed on light microscopy, phase-contrast and electron microscopy. The cytoplasmic inclusions were found to consist of a laminated shell containing dense particles 3-14 μ in diameter. R. LOVE (pp. 101-117) studied infections of the same cells with Bunyamwera, NDV, Coxsackie and other viruses: with Bunyamwera RNA inclusions in the nucleus appeared; with NDV and Coxsackie phospholipid concentrations in the Golgi zone appeared into which RNA protein was apparently extruded from the nucleus.

T. F. McNAIR SCOTT and D. L. McLEOD (pp. 118-128) described 2 strains of herpes virus one of which produced syncytial giant cells in HeLa cultures while the other caused proliferation and piling up of cells without fusion. M. G. P. STOKER and ALISON NEWTON (pp. 129-132) found that a strain of herpes virus caused inhibition

of mitosis in HeLa cells when infected 90 minutes or more before division.

Sarah A. LUSE and Margaret G. SMITH (pp. 133-144) described electron microscopy of human uterine fibroblasts infected with salivary gland virus, and W. G. BANFIELD and Darlene C. BRINDLEY (pp. 145-163) similar studies of the lesions of molluscum contagiosum and the causative virus particle. D. L. COFFIN (pp. 164-171) used fluorescent antibody to demonstrate virus antigen in the cytoplasmic and nuclear inclusions of canine distemper virus and to show that it infects most of the cell types in the body.

Sonja M. BUCKLEY (pp. 172-187) has developed a haemagglutination-haemadsorption technique for Kyasanur Forest disease virus in S_3 -HeLa cells and has studied cytopathic effects in several cell-systems caused by a wide range of arthropod-borne viruses.

The last 4 papers discuss the main difficulties in study of the cytopathology of virus infections: W. W. ACKERMANN (pp. 188-192) the biochemical aspects, Chien LIU (pp. 193-196) the relationship of viral antigen to inclusion bodies, C. G. HARFORD, Alice HAMLIN and Esther P. RODERMUND (pp. 197-206) the difficulties of interpretation in electron microscopy, and H. PINKERTON (pp. 207-213) the relation of viruses to inclusion bodies, studies of the effects of radiation on viral multiplication, and rickettsial multiplication.

[These papers contain a wealth of detail and illustrations which is not easy to summarize.]

C. E. Gordon Smith

MATUMOTO, M., MUTAI, M., AOYAMA, Y. & OIKAWA, T.
HSO Virus: an Apparently New Cytopathogenic Virus isolated in HeLa Cell Culture from Normal Human Serums. *Japanese J. Exper. Med.* 1960, June, v. 30, No. 3, 213-26, 2 text figs. & 8 figs. on pl. [21 refs.]

This paper from Tokyo describes the isolation of a new virus called HSO (Human Serum Orphan) virus. This virus was isolated in HeLa cells from 3 batches of human serum from individual donors. It produced cytopathic effects in the HeLa cells and could be passed indefinitely in series. It could be filtered through bacteria-proof filters but could be centrifuged out of suspension by 80,000 g. The virus was resistant to ether. It grew well in HeLa cells, human embryo cells and several other continuous cell lines but it produced no cytopathic effects in monkey kidney cell cultures although some limited propagation of the virus may have occurred. The virus did not grow in chick embryo tissue cultures. Similarly, it was not pathogenic for suckling mice, adult mice, guinea-pigs, rabbits, monkeys or embryonated eggs. The viruses isolated from the 3 sera were antigenically closely related. Serological evidence that they infect human beings was obtained. The virus appeared to be antigenically distinct from other viruses studied in these laboratories. It was tested against influenza, HVI, Japanese encephalitis, herpes, vaccinia, and Rift Valley fever viruses. It was later tested against the 3 types of poliomyelitis virus, against some of the ECHO viruses (types 1-7, 9 and 12), some of the Coxsackie viruses (Group A types 11, 13, 15 and 18) and types 1 to 14 of

the adenoviruses. It is concluded that a new virus has been isolated from human serum. As yet there is no knowledge of the disease, if any, that results from infection by this virus. [It was found that after 12 minutes at 56°C. no virus could be detected in a sample that originally contained more than 10⁶ TCD50. In the original isolations the human serum used for the growth of HeLa cells had been inactivated at 56°C. for half an hour. There are many possible explanations for this discrepancy but the matter is not discussed at all in the paper.]

A. J. Beale

MORZYCKA, Maria. **Isolation of the Cytopathic Agent from Calf Serum.** *Bull. Inst. Marine Med. Gdańsk.* 1960, v. 11, Nos. 1/2, 61-3, 2 figs. on 2 pls.

Biological media used for tissue culture, which cannot be sterilized by heat, are a potential source of viral contamination. The recovery of a virus from calf serum used to grow the Fl. strain of human amnion cells is described. The virus produced cytopathic effects similar to herpes or vaccinia viruses but was not positively identified. It resisted 56°C. for 1 hour but was destroyed by 60°C. for 1 hour. The virus could pass through a Seitz filter. The necessity for vigilance to prevent confusion from isolates is stressed.

A. J. Beale

KATO, S., TAKAHASHI, M., KAMEYAMA, S. & KAMAHORA, J. **A Study on the Morphological and Cyto-Immunological Relationship between the Inclusions of Variola, Cowpox, Rabbitpox, Vaccinia (Variola Origin) and Vaccinia IHD and a Consideration of the Term "Guarnieri Body".** *Biken's J.* Osaka. 1959, Dec., v. 2, No. 4, 353-63, 47 figs. (44 on 10 pls.) [25 refs.]

A comparative study has been made of the inclusions produced by certain pox viruses in HeLa and FL cells and in the cells of the chorioallantoic membrane. Two types of intracytoplasmic inclusion bodies, designated types A and B, were seen in the tissue culture cells. In preparations fixed with methanol and stained with Giemsa type A inclusions appeared as small round bodies stained pale blue, whereas type B inclusions were stained reddish purple and developed from small compact bodies to large diffuse granular networks. After fixation with Bouin and staining with haematoxylin and eosin the type A inclusions were red and both types were surrounded by halos. Type A inclusions were produced by cowpox and ectromelia, but not by variola, rabbitpox or vaccinia; all the viruses produced type B inclusions. In the cells of the chorioallantoic membrane there were type A inclusions but inclusions of type B could not always be distinguished. In a concluding discussion the authors consider that the Guarnieri body is a type B inclusion and Marchal and Bollinger bodies are type A inclusions.

D. J. Bauer

MAYR, A. & HERRLICH, A. **Züchtung der Variolavirus in der infantilen Maus. [Development of Variola Virus in Baby Mice]** *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 2, 226-35, 3 figs. [32 refs.]

Material from lesions of smallpox patients can be transmitted to baby mice. During 20 intraperitoneal passages in mice the characteristics of the virus in chick embryo chorio-allantoic membrane remained unchanged. The behaviour in mice, however, changed during passage. The mice of the first passage all died in 3 to 8 days with ascites and other changes, and virus was isolated from lungs, kidneys, liver and spleen, the highest titres being found in lungs and kidneys. Between 4th and 10th passages all animals lived. Those killed on the 7th post-inoculation day had a fair amount of virus in their lungs, but little or none in the other organs investigated. By the 32nd day there was very little virus in the lungs and none elsewhere. In subsequent passages mortality increased until in the 19th and 20th more animals died between the 5th and 8th days than lived to the 21st day. The dead showed ascites and hydrothorax, and virus was recovered from all the organs investigated. The minority of animals still alive on the 21st day all had virus in the lungs, some in the kidneys and none in the liver and spleen. In some animals which showed no signs of illness after inoculation, virus was isolated from the lungs (but not from other organs), as long as 45 days later.

Colin Kaplan

MARENNIKOVA, S. S., GURVICH, E. B. & YEMASHEVA, M. A. **Isolation and Study of the Properties of Smallpox Virus. I. Direct Isolation of Smallpox Virus in Tissue Cultures.** *Problems of Virology.* London. 1959, v. 4, No. 6, 70-77, 4 figs. [15 refs.] [Translated from Russian.]

Vesicular fluids and crusts from patients with smallpox were used in this investigation to infect human embryonic skin-muscle cultures and cultures of Hep-2 cells. It was found that cytopathic changes became obvious by low-power microscopy from the 3rd day in some isolation attempts, but not until the 6th or 7th day in others. Examination of stained cover glass preparations showed cytoplasmic inclusions by the 2nd day. The specificity of the cytopathic changes was shown by the action of antivaccinial gamma globulin in neutralizing them. Adsorption of vaccinia-sensitive fowl erythrocytes to foci of virus-infected cells could be seen before cytopathic changes were visible by low-power microscopy.

In a series of parallel inoculations of tissue cultures and chick embryo chorio-allantoic membranes, 5 out of 6 attempts were successful in 1st passage tissue cultures. All 6 attempts were successful in chorio-allantoic membranes, one in the second passage, and another (negative in tissue culture) at the 4th passage.

Colin Kaplan

BONITZ, K. & SEELEMANN, K. **Pockenimpfstoff aus Gewebekulturen. [Smallpox Vaccine from Tissue Culture]** *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 2, 236-52, 2 figs. [29 refs.]

The authors used trypsinized bovine embryo skin, bovine embryo muscle and chick embryo skin and muscle cells to grow vaccinia virus. Bovine embryo muscle and chick embryo skin and muscle cells gave them most virus 30 hours after inoculating their cultures. The optimal

cell concentration was 2×10^6 per ml., and Parker's medium 199 + serum (2 to 20%) was more effective than either unsupplemented 199 or bovine amniotic fluid. They, too, found that about 90% of the virus was associated with the cells.

Smallpox vaccine prepared from this virus showed satisfactory stability when stored at 4°C. and -20°C., and in clinical trials gave about 97% "takes" in primary vaccinations. In re-vaccinations vesicular and pustular reactions were about 36%. [The rather low "take" rate in re-vaccination may be explained by the vaccine titres, which were between 10^7 and 3×10^7 i.u./ml. At this level of potency one may expect a low re-vaccination "take" rate accompanied by a perfectly satisfactory primary "take" rate.]

Colin Kaplan

WIGAND, R. & NIELSEN, G. Zur Frage der Existenz löslicher und virusgebundener Anteile von komplementbindendem Antigen und Hämagglutinin des Vaccinevirus. [The Question whether there are Soluble and Virus-Bound Components of Complement-Fixing Antigen and Haemagglutinin of Vaccinia Virus] *Arch. f.d. gesamte Virusforschung*, 1960, v. 10, No. 2, 215-25. [20 refs.]

Vaccinia virus from rabbit skin was subjected to successive centrifugations at 6,000 g after resuspension of the sediments in fresh suspending fluid. The supernatants showed steadily diminishing titres of both complement-fixing (CF) antigen and haemagglutinin (HA). Storage of a washed virus suspension at 4°C. for 7 days was followed by a 4-fold rise in HA, and for 14 days by an 8-fold rise in the CF antigen. There was no significant change in the virus infectivity after 4 centrifugations. Materials from HeLa cells infected with vaccinia virus behaved similarly. The authors conclude that there is probably not any virus-bound HA [although their results do not altogether bear this out], and that the CF antigen is associated with the virus particle, which cannot be washed completely free of it [CRAIGIE and WISHART, this *Bulletin*, 1937, v. 12, 230].

Colin Kaplan

CANTELL, K. & TOMMILA, V. Effect of Interferon on Experimental Vaccinia and Herpes-Simplex Virus Infections in Rabbits' Eyes. *Lancet*, 1960, Sept. 24, 682-4. [11 refs.]

Interferon has been shown to inhibit the growth of a number of viruses in tissue culture and in the chick embryo, and also to inhibit the growth of vaccinia in the skin of rabbits [this *Bulletin*, 1958, v. 33, 188; 1960, v. 35, 200]. Another example of inhibition of virus multiplication *in vivo* by interferon is reported here.

Interferon was prepared by incubating rabbit kidney cell cultures with UV-irradiated mumps virus. Fluid from cultures incubated with normal allantoic fluid was used as a control. Vaccinia virus was dropped onto the corneas of 6 rabbits and interferon was then applied to the right eye and control fluid to the left. For the next 4 days, more interferon was applied 6 times daily. (Interferon itself caused no toxic effects.) In the eyes treated with interferon infection developed 4 days later than in

the control eyes, the disease was milder and the lesions smaller. The possibility of reinfection from the control eye could not be excluded. It appeared that interferon had reduced, if not inhibited altogether, the multiplication of vaccinia in the rabbits' eyes.

When the experiments were repeated with 5 rabbits inoculated with herpes simplex no consistent differences between eyes treated with interferon and controls were observed. Infection with herpes was more severe than with vaccinia. Other workers have found that herpes growing in chick chorioallantoic membranes [ISAACS *et al.*, *ibid.*, 1959, v. 34, 291] and in tissue cultures [HO and ENDERS, *ibid.*, 1960, v. 34, 516] is not inhibited by interferon.

Janice Taverne

WHEELER, C. E., with the technical assistance of C. M. CANBY. Herpes Simplex Virus. Characteristics of a Strain which produces Unusually Large Multinucleated Giant Cells in Tissue Culture. *Arch. Dermat.* 1960, Sept., v. 82, No. 3, 391-7. [10 refs.] Discussion 397-9.

Plaques made by the HF strain of herpes simplex in HeLa cells normally consist of small multinucleate cells, usually with less than 50 nuclei, and rounded cells lying singly or in clumps. After 17 subcultures in HeLa cells growing in a medium containing neutralizing antibody, a variant (HPF) producing a plaque made up of large syncytial giant cells with several hundred nuclei was observed. The variant still produced the same kind of plaques in the absence of antibody. It was neutralized by herpes antiserum. HPF virus was much less pathogenic for animals than the HF strain. In rabbits it stimulated the production of high levels of neutralizing antibody but caused only a mild kerato-conjunctivitis whereas the HF strain caused severe lesions, frequently followed by encephalitis and death. Mice inoculated intracerebrally with the HPF strain had a lower mortality rate and deaths occurred several days later than with the HF strain.

It is suggested that on account of its markers, decreased virulence for animals and distinctive plaque morphology, the HPF strain may be useful in genetic work.

Janice Taverne

SCHMIDT, Nathalie J., LENNETTE, E. H. & SHON, Carol W. A Complement-Fixing Antigen for Herpes Simplex derived from Chick-Embryo Tissue Cultures. *Amer. J. Hyg.* 1960, July, v. 72, No. 1, 59-72, 2 figs. [12 refs.]

Herpes simplex virus grown in tissue cultures of chick embryo fibroblasts had a higher titre than when grown in HeLa, FL human amnion or monkey kidney cells. The conditions required for the production of the most potent complement-fixing (CF) antigen from the fibroblasts were therefore investigated. The procedure adopted was to incubate infected cells for 48 hours in a medium containing lamb serum and lactalbumin hydrolysate and then to disrupt them by freezing and thawing. This suspension was used unconcentrated and without removing cellular debris.

Convalescent sera from 76 patients from whom virus had been isolated gave the same results in CF tests with this antigen and an antigen prepared from infected chorioallantoic membranes. Serum titres with the 2 antigens never differed by more than 2-fold, and the tissue culture antigen was the more specific. Only 1 out of 228 sera reacted with antigen prepared from uninfected fibroblasts, whereas 59 reacted with an antigen made from uninfected eggs.

About half the CF activity of the egg antigen sedimented with the infective particles on high-speed centrifugation, while half (soluble antigen) remained in the supernatant fluid. With the tissue culture antigen, less activity remained in the supernatant fluid, suggesting either that the size of the CF particle or the amount of soluble antigen bound to sedimentable material varied with the host tissue employed. Several other workers have reported that complement-fixation with herpes occurs with a soluble antigen. This was confirmed in that (i) a preparation of infective particles could be obtained which did not fix complement, and (ii) high-speed centrifugation of soluble antigen did not reduce its CF activity although it reduced its infectivity by 99%.

Janice Taverne

MAASS, G. & MANNWEILER, K. Cytologische und biologische Untersuchungen über das Verhalten des Mumps-Virus in Affeniernepithelkulturen. [Cytological and Biological Investigations of the Behaviour of Mumps Virus in Monkey Kidney Epithelial Cell Cultures] *Arch. f.d. gesamte Virusforschung*. 1960, v. 10, No. 2, 195-207, 8 figs. [28 refs.]

The Po strain of mumps virus has been grown in cultures of trypsinized monkey kidney cells. New virus appeared 24-48 hours after infection and attained a titre of $10^{4.5}$ - $10^{4.7}$, which persisted at the same level for 3 days. A cytopathic effect appeared after 48-72 hours, and consisted of the formation of giant cells with eosinophilic intracytoplasmic inclusions. Haemadsorption with chick, human, rhesus, guineapig and sheep red cells could be observed 40-50 hours after infection. Preliminary treatment of the cultures with receptor-destroying enzyme did not affect the subsequent course of the infection.

D. J. Bauer

CANTELL, K. & PENTTINEN, K. Role of Inhibitors in Hemagglutination Behavior of Mumps Virus. *Proc. Soc. Exper. Biol. & Med.* 1960, July, v. 104, No. 3, 488-90, 3 figs. [15 refs.]

The authors have investigated the haemagglutination produced by 4 strains of mumps virus. Allantoic fluids infected with the Enders strain gave haemagglutination titres with human and chick red cells similar to that obtained with a pool of the same fluids, whereas with the Habel strain the titre of the pool was much lower than the individual titres, an effect which was ascribed to the presence of an inhibitor in some of the fluids. The KS and Chopin strains also behaved irregularly.

(L. 154)

Various methods were employed for the purpose of destroying the postulated inhibitor, and it was found that fluids which failed to agglutinate human red cells would do so after ultrasonic irradiation, ultracentrifugation, treatment with receptor-destroying enzyme, dialysis against buffered saline, or incubation at 35°C. for 2 days.

D. J. Bauer

MAXIMOVICH, N. A. & MITCHENKO, V. P. Study of Cellular and Viral Nucleic Acids in Experimental Influenza Infection using Fluorescence Microscopy. *Acta Virologica*. Prague. 1960, July, v. 4, No. 4, 227-32, 4 coloured figs. on 2 pls. [15 refs.]

Mice were inoculated intranasally with 1,000 LD50 of PR8 virus and killed at intervals. Impression smears from the lungs and upper respiratory tract were stained by immersion, without fixation, in acridine orange 1/20,000 in phosphate buffer pH 7.2-7.4 and examined in blue-violet light. The authors describe the appearance of red-staining "inclusions" within 3 hours after infection, which were found in bronchial cells for up to 5 days and alveolar cells for up to 2 weeks. [1,000 LD50 should kill the mice within 10 days.] They think the first changes were due to phagocytosis of RNA in the inoculum and that later changes were due to virus multiplication. [It is stated in the methods section that the cells were photographed but the illustrations seem to be rather poor paintings.]

[See also this *Bulletin*, 1956, v. 31, 217, *bis.*; 1957, v. 32, 229; 1958, v. 33, 530.]

D. A. J. Tyrrell

AMELUNXEN, R. E. & WERDER, A. A. Quantitative Considerations of Influenza Virus Neutralization. I. Number of Antibody Molecules per Virus Particle. *J. Bacteriology*. 1960, Aug., v. 80, No. 2, 271-7, 1 fig. [15 refs.]

Hyperimmune rabbit serum was prepared by inoculating rabbits with purified influenza A (PR8) virus and Freund's adjuvant. This serum, undiluted, was sufficiently potent completely to neutralize purified and concentrated virus ($10^{10.77}$ ID50/ml.) when both were mixed in equal proportions at 25-27°C. for 2 hours and 4°C. for 16-18 hours. After incubation, samples were withdrawn for protein analysis (Nessler procedure) and determination of virus activity. There was no detectable dissociation of virus by ultracentrifugation (65 minutes at 37,500 r.p.m.) or by dilution. Virus-serum mixtures were ultracentrifuged and the amount of protein nitrogen remaining in the supernatant was determined; the quantity of specific antibody nitrogen adsorbed from the mixture, and from this the amount of antibody protein, was calculated. The assumption was then made that the antibody was gamma globulin and 160,000 was taken as the molecular weight (replicate experiments with gamma globulin fractionated from rabbit whole serum gave comparable results, lending strong evidence that the use of 160,000 was valid) and, using this figure, the authors calculated the total number of antibody molecules bound per total virus used. The number of virus particles

present in the purified virus preparation was determined from electron micrographs and the average number of molecules bound per virus particle was found to be 6,040. Successive adsorptions of whole serum and gamma globulin showed a progressive decrease in the number of antibody molecules adsorbed; at a point where virus activity was beginning to be demonstrable, about 1,200 antibody molecules were bound per virus particle.

The authors postulate that 1,200 is the maximal number of antibody molecules required for the inactivation of one or more critical sites on an influenza virus particle and that the statistical probability of one antibody molecule inactivating an influenza virus particle would be low.

[The authors have calculated the number of molecules required to inactivate virus under the conditions of complete and > 99% neutralization. It is probable that the average number of antibody molecules on a virus particle when, for example, 95% of particles are neutralized is substantially less than the figures given.]

D. Taylor-Robinson

BLASKOVIC, A. D. [Edited by.] Otázky experimentálnej patogenity a rezistencie organizmu voči chrípkovkej infekcii vírusmi zo skupin A-FE (tzv. dzijskými). [Experimental Pathogenicity of and Resistance to A-FE Influenza Viruses (the So-Called Asian Influenza)]. *Biologické Práce*. Bratislava. 1958, v. 4, No. 11, 117 pp., illustrated. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The team of research workers of the Institute of Virology of the Czechoslovak Academy of Sciences involved in research on the problem: 'Biology and Biochemistry of the Influenza Virus Infection' decided to undertake investigations concerning some properties of recently isolated strains of influenza virus of the A-FE group (type A—Far East). Their attention was concentrated onto these questions: the reason for the high pathogenicity of these viruses for man and the process of adaptation of them to new species of animals. Strains of A-FE viruses were therefore tested from the point of view of their possible special toxic properties, their ability of exhibiting cytopathogenic effect, the formation of antibodies against them and the properties of the antibodies. Results on their morphology and some physical and biological properties complete the investigations.

"The establishing of the level of antibodies in human sera from individuals of various age-groups was important from the point of view of judging the state of immunity of our population against infections with viruses of the A-FE group as well as with viruses of the B type. These findings brought valuable results already in the past for the understanding of the epidemiological process.

"In some of the papers the properties of the A-FE viruses are compared not only with viruses of the A type of human origin but also with new strains of viruses isolated in 1956 in Czechoslovakia, namely strain A anatis/Košice/1956 from ducklings and strain A equi/

Praha/1956 from a horse. The summaries of the individual papers follow."

ISAACS, A. & BARON, S. Antiviral Action of Interferon in Embryonic Cells. *Lancet*. 1960, Oct. 29, 946-7, 1 fig.

The authors have attempted to produce interferon in cultures of tissues taken from chick embryo of varying periods of inoculation and treated with influenza virus irradiated with UV light. They find the yield of interferon is highest with tissue taken from embryos aged 15 days and lowest with tissues from embryos aged 6 days (the earliest tested). Similar results were obtained by using tissue from mouse embryos of various periods of gestation. It is suggested that these findings might be related to the changes in metabolism of the cells at different stages of embryonic development, and might indicate that after 3 months' gestation human embryos are not damaged by maternal infections with rubella virus because they can then produce interferon.

D. A. J. Tyrrell

HOBSON, D. & SCHILD, G. C. Virological Studies in Natural Common Colds in Sheffield in 1960. *Brit. Med. J.* 1960, Nov. 12, 1414-18, 1 fig. [10 refs.]

The authors have attempted to repeat and amplify the experiments of workers from the Common Cold Research Unit, Salisbury [this *Bulletin*, 1960, v. 35, 616, *ter*], who claimed to have isolated cytopathic viruses from common colds by inoculating cultures of human embryo kidney cells incubated with rolling at 33°C. and with a low (0.35 gm./litre) concentration of sodium bicarbonate in the medium. Using these (CC) conditions (but with bicarbonate at 0.52 gm./litre) the present authors propagated *in vitro* and isolated from volunteers one of the Salisbury strains (HGP). Propagation and isolation were unsuccessful in the conditions commonly used for routine virus diagnosis. However certain representative viruses of other groups, such as influenza, adenoviruses and Coxsackie viruses were found to grow in both routine and CC conditions. Using CC conditions the authors isolated viruses from 8 of 25 washings taken from patients in the early stages of common colds. One of these viruses (30/60) would grow in monkey and human embryo kidney cells, the others grew only in human embryo kidney cells. The results with 30/60 and one of the latter group (16/60) are described in detail. Preliminary serological evidence indicates that these two viruses are serologically distinct from each other and from HGP. In CC conditions HGP and 30/60 strains apparently multiplied and caused a cytopathic effect in H.Ep II cells, but strain 16/60 did not.

[An annotation in the same issue, p. 1439, points out that there have been at least 5 reports of cultivation of common cold viruses which have not been confirmed by subsequent work but that the present paper provides "very full confirmation" of the claims of the Salisbury workers.]

D. A. J. Tyrrell

TOSI, H. C. & RODRIGUEZ MARTINEZ, R. J. Multiplicación de los poliovirus sobre cultivos *in vitro* de músculos esqueléticos de ratones lactantes. [The Multiplication of Poliomyelitis Virus in Cultures of Infant Mouse Skeletal Muscle] *An. Facul. de Med. Montevideo*. 1960, v. 45, No. 1, 56-61, 8 figs. English summary.

Fragments of skeletal muscle of mice 2-3 days old were grown in tubes containing a medium consisting of 40% bovine amniotic fluid, 10% bovine embryo extract, 15% horse serum and 35% Hanks solution with antibiotics, which was renewed every 2 days. After incubation for 48 hours the fragments were surrounded by a zone of growth containing fibroblasts, muscle fibres and macrophages. Explants with a diameter of 2-4 mm. were infected with poliomyelitis virus and then maintained in a medium consisting of 50% bovine amniotic fluid, 5% horse serum and 45% Hanks solution with antibiotics. All 3 types of poliomyelitis virus produced a cytopathic effect which was maximal after 6-8 days. The cultures were successfully used for isolating and identifying type 1 virus from the stools of patients suffering from poliomyelitis.

D. J. Bauer

KHESIN, I. E. & GULEVICH, N. E. Karyometric Investigation of the Cytopathic Effect of Poliomyelitis Virus in Leukaemic Cell Cultures. *Acta Virologica*. Prague. 1960, Sept., v. 4, No. 5, 311-19, 7 text-figs. & 5 figs. on 2 pls. [24 refs.]

The surface area of the nuclei of the Oregon J-96 cell strain (OSGOOD and BROOKE, *Blood*, 1955, v. 10, 1010) growing as monolayers on mica sheets was determined for normal cells and cells infected with poliomyelitis virus. It was found that the nuclei from infected cultures had a larger surface area. The enlargement of the nuclei was observed after 1 hour but there was no progressive increase in size. It was also found that the degree of enlargement of the nuclei did not depend upon the virus dose in the range of 10-500 TCD of virus. [The multiplicity of infection is not given.] No evidence of increased cell growth could be found and the increased size of the nucleus is called disintegrative swelling to distinguish it from the functional swelling of nuclei which is seen during increased specific activity or growth of cells.

A. J. Beale

CARP, R. I., KRITCHEVSKY, D. & KOPROWSKY, H. Effects of Deuterium Oxide upon Poliovirus Multiplication. *Virology*. New York. 1960, Sept., v. 12, No. 1, 125-7.

It was found that the yield of CHAT type 1 poliovirus was increased about 10-fold in monkey kidney cells grown in deuterium oxide (D_2O) instead of H_2O at 37°C. Similar results were obtained with HeLa cells clone S3. It was also found that the yield of this poliovirus at 40°C. in D_2O approached within 10-60% of that at 37°C., whereas in H_2O very low titres were produced at this temperature. The progeny of virus grown at 40°C. in

(L. 154)

D_2O was found to grow considerably better even in ordinary media at 40°C. than virus grown at 37°C.

A. J. Beale

PRINZIE, A., SCHONNE, E. & DE SOMER, P. Inactivation et spécificité cellulaire de l'acide ribonucléique du poliovirus. [Inactivation and Cellular Specificity of Poliovirus Ribonucleic Acid] *Arch. f.d. gesamte Virusforschung*. 1960, v. 10, No. 2, 153-66, 3 figs. [25 refs.]

This is an interesting paper about the infectious RNA extracted from poliomyelitis virus by the phenol method of GIERER and SCHRAMM (*Ztschr. Naturforsch.*, 1956, v. 11b, 138). First it is shown that the activity of ribonuclease decreases with increasing molarity of salt solution. In this work 1 M NaCl was used for the RNA inoculated onto cells. RNA extracted from poliomyelitis virus inactivated by formalin, β -propiolactone or ultraviolet light was found not to be infectious. Doses of phenol that inactivated poliomyelitis virus preparations were found to destroy the antigenicity. This demonstrates that the action is on the protein part of the virus since, of course, the phenol extraction method does not harm the nucleic acid. RNA extracted from virus neutralized by specific antiserum was infectious. Finally, experiments were done on the activity of RNA on cells not susceptible to infection with intact poliomyelitis virus. It was found that these cells, intact chick embryos and 2 cell lines derived from a pure line of rat R (these cells are called DE 40 and DE 7 and are derived from mammary tumours induced by acetyl-amino-fluorine) produced intact poliomyelitis virus when infected with poliomyelitis virus RNA. One of the cells, DE 40, in the first 18 hours produced as much virus as HeLa cells when both were infected with RNA. It was also found that the infectious RNA was readily destroyed by heat at 37°C., no infectivity being left after 6 hours.

A. J. Beale

NORMAN, A. & VEOMETT, R. C. Heat Inactivation of Poliomyelitis Ribonucleic Acid. *Virology*. New York. 1960, Sept., v. 12, No. 1, 136-9, 2 figs.

Heat inactivation of the RNA extracted from MEF 1 type 2 poliovirus by the method of GIERER and SCHRAMM was found to follow first order kinetics in the temperature range 40-70°C. at pH 7.2 down to 1% survival. The heat and entropy of activation were respectively 31 kcal./mole and 21 cal./mole/degree. [FRENCH and ARMSTRONG (this *Bulletin*, 1960, v. 35, 938) found the heat inactivation energy in the range 47°C.-55°C. for inactivation of intact type 2 poliovirus was 202 kcal./mole.] The experiments were done both in 1.2 M and 0.12 M NaCl and there was a 2-fold lower rate of inactivation in the stronger salt solution. Also in this solution at temperatures below 60°C. there was an initial shoulder in the inactivation curve thought likely to be due to RNA aggregation. At high temperatures it is noted that intact poliovirus is much more readily inactivated than its RNA [but see MEDEARIS *et al.*, *ibid.*, 1250]. Also the RNA of poliovirus is much more heat-sensitive than that of tobacco mosaic virus.

A. J. Beale

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LOW, R. J. & BARON, S. **Poliovirus Inhibitor from the Central Nervous System of the Rhesus Monkey.** *Science*. 1960, Sept. 2, v. 132, 622-3.

Virulent type 1 poliovirus can be isolated from the central nervous system of all monkeys that show histological evidence of poliovirus infection. By contrast virus was only isolated from 30% of samples of CNS tissue showing histological evidence of poliovirus infection after the injection of attenuated strains. It was found that there is present in CNS tissue an inhibitor of poliovirus. This substance is present in normal CNS suspensions and is not a product of virus cell interaction. It is equally active against all 3 types of poliovirus and against virulent and attenuated strains. It is not active against Coxsackie A9 or ECHO 12. The inhibitory substance is inactivated at 56°C. in 30 minutes, stable at -20°C. for 4 months, sedimented at 1,000 r.p.m. for 30 minutes [precise *g* required not given], and not dialysable. The explanation for the failure to isolate attenuated and the success with virulent viruses from the CNS, when both are equally susceptible to the inhibitor, probably lies in the fact that virulent viruses grow to higher titre in the CNS.

[It is a common observation that polioviruses are not readily isolated from the CNS of fatal cases of poliomyelitis. This is presumably due to an inhibitor similar to that found in monkey CNS suspensions described above. The inhibitor may sometimes be diluted out.]

A. J. Beale

CHUMAKOV, M. P., GAGARINA, A. V., LASHKEVICH, V. A., DZAGUROV, S. G., RAL'F, N. M., FLEER, G. P., VOROSHILOVA, M. K. & ROBINSON, I. A. **Comparative Characteristics of Live Poliomyelitis Vaccine prepared in the Institute for the Study of Poliomyelitis of the U.S.S.R. Academy of Medical Sciences, and Sabin Vaccine from Attenuated Strains of Poliomyelitis Virus.** *Problems of Virology*. London. 1959, v. 4, No. 5, 20-24. [Translated from Russian.]

A brief account of the method of preparing attenuated poliovaccine from seed virus provided by Dr. SABIN is given. Virus was grown on monkey kidney cells and 10% were used as controls for simian viruses. Sterile lots were filtered and the filtrates tested in animals for lymphocytic choriomeningitis, Coxsackie and Virus B. Results of testing Russian attenuated vaccine and Sabin's seed for neurovirulence are shown. Intracerebrally no paralysis or histological lesions were produced. Intraspinal paralysis and histological lesions were produced with all 3 strains, with both Sabin's seed and Russian vaccine. For type 1 virtually all animals showed lesions and most showed paralysis. The course of the disease and extent of the histological lesions suggests, however, that the Sabin strains are not capable of causing a generalized infection. The vaccine was found to be stable at room temperature for 7-12 days.

[This is a general rather than a detailed account.]

A. J. Beale

ANDZHAPARIDZE, O. G. & SOLOV'EV, V. D. **The Scientific Basis for the Production of Inactivated Poliomyelitis Vaccine.** *Problems of Virology*. London. 1959, v. 4, No. 5, 25-34, 4 figs. [19 refs.] [Translated from Russian.]

This is a general review of manufacturing experiences with killed poliovaccine in the U.S.S.R. Consideration was given to the development of successful methods of producing trypsinized monkey kidney cells. A yield of 50×10^6 cells per gramme of kidney was finally achieved. A casein hydrolysate medium was used for cell growth and medium 199, without 35 of its 64 constituents, was used for virus growth. The immunogenic index (ratio TCD50/antigen extinction titre) for various strains of poliovirus was determined. It was found that the Brunden type 1 strain (as used in England), the MEF 1 type 2 strain (also as used in England) and the Saukett type 3 strain (as used in Denmark) were the most immunogenic. Investigations were also carried out into methods of filtration. It was found that the grade of pad used was important but that pretreatment with gelatin prevented virus adsorption to a great degree. The second filtration was found to remove more vaccine potency than the first one. The authors believe that the question of removing this step should be reopened and note that already in some countries this requirement has been relaxed. [It may be noted that although some manufacturers have experienced trouble with this filtration step others have overcome it.] Formalin alone causes very little loss of potency. For testing the potency of final vaccine the authors advocate the use of white rats in preference to monkeys. They are cheaper, hardier, and give more consistent results. Moreover, sufficient animals can be used to give a valid test. The vaccine produced in Russia has proved consistently safe, no virus being isolated in safety tests. Cell lines have been investigated for safety tests. HeLa cells are 10-100 times less sensitive, SOT (cynomolgus monkey heart) cells equally sensitive and HEP-2 10-100 times more sensitive than monkey kidney cells. The vaccine could also be made satisfactorily from virus grown in SOT cells.

A. J. Beale

FUJITA, T., SUGAI, T. & OKUNO, Y. **Cultivation of Coxsackie Virus (Group A, Type 2) in Mouse Tissue Grafted to Chorioallantois.** *Biken's J.* Osaka. 1959, Dec., v. 2, No. 4, 295-303. [13 refs.]

Coxsackie A2 virus was successfully adapted to grow on the chorioallantoic membrane by prior passage (11 or 12 generations) in adult mouse muscle grafted on the chorioallantoic membrane. The use of adult mouse kidney grafts was not successful. The virus grown on the chorioallantoic membrane was back titrated in mice and shown serologically to be still Coxsackie A2. Challenge of Coxsackie A2 infected chick embryos with mumps virus demonstrated interference by a reduction in haemagglutinin titre.

A. J. Beale

FRANKLIN, A. E. **The Effect of Hormones on HeLa Cells inoculated with Infectious Hepatitis Specimens.** *Canadian J. Microbiol.* Ottawa. 1960, Oct., v. 6, No. 5, 529-33. [24 refs.]

"HeLa cells have been studied in media supplemented with prednisolone, hydrocortisone, testosterone, oestradiol, progesterone, and aldosterone, singly and in combination. Twelve acute phase infectious hepatitis specimens did not cause a consistent degenerative effect in hormone-enriched cultures. Repeated inoculation with two virus specimens to cultures with testosterone also failed to produce a cytopathogenic effect."

ACKERMANN, R., with the technical assistance of Hildgard FUCHS & Steffi KROEHNERT. Über die Züchtung des Virus der lymphocytären Choriomeningitis in Mäuseembryo-Zellkulturen. [Cultivation of Lymphocytic Choriomeningitis Virus in Mouse Embryo Cell Cultures] *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 2, 183-94, 2 figs. [22 refs.]

Trypsinized cultures of the tissues of embryo mice at the 12th-18th days of gestation were grown in a medium consisting of Hanks solution with 0.5% lactalbumin hydrolysate, 0.1% yeast extract, 0.45% glucose, 0.01% L-glutamine, 0.001% L-valine and 10 or 20% calf serum. The WE3 strain of lymphocytic choriomeningitis virus multiplied in the cultures, and could be made to produce a cytopathic effect by varying the composition of the medium used after infection. Satisfactory results were obtained with a mixture of 47.5% growth medium, 50% bovine amniotic fluid and 2.5% horse serum; the virus could be maintained through 12 passages, attaining titres of up to 10^7 , and produced a cytopathic effect involving 50-90% of the cell sheet. The affected cells became rounded and detached from the glass. The identity of the virus was confirmed after 4, 6 and 10 passages by neutralization tests. *D. J. Bauer*

ŘEHÁČEK, J. & PESEK, J. **Propagation of Eastern Equine Encephalomyelitis (EEE) Virus in Surviving Tick Tissues.** *Acta Virologica.* Prague. 1960, July, v. 4, No. 4, 241-5, 9 figs. [12 refs.]

The Cg strain of eastern equine virus in its 28th mouse passage was used in various arthropod tissues surviving in medium 199 at 25°C. Virus titrations were made by a pH test in chick embryo fibroblast cultures. Various tissues from *Dermacentor pictus* were compared but multiplication occurred only in fat-body with hypodermis. When 10^4 TCD50 were inoculated the virus persisted almost without loss of titre for 6 days; when $10^{2.5}$ TCD50 were inoculated multiplication occurred; with less than $10^{0.6}$ TCD50 inoculated a maximum titre of $10^{-4.3}$ was reached on the 9th day. In other tissues the virus tended to survive longer than in medium with-

out tissue. In fat-body with hypodermis of *Ixodes ricinus* a slow fall of titre occurred with inocula of 10^4 and $10^{2.5}$ TCD50, but marked multiplication to $10^{-3.3}$ on the 11th/12th days occurred after inoculation of $10^{0.6}$ TCD50. In all tissues of *D. marginatus* there was a slow fall of titre although survival was longest in fat-body with hypodermis. In the fat-body and hypodermis of a cockroach (*Periplaneta americana*) the virus lost titre at the same rate as in medium without tissue. Newcastle disease virus did not multiply but survived longer than in medium without tissue, in tissues of *D. marginatus* and *I. ricinus*. *C. E. Gordon Smith*

KOVAC, W. Histologische Veränderungen des befruchteten Hühneries nach Infektion mit dem Virus der Frühsommer-Meningoencephalitis (FSME). [Histological Changes in Embryonated Chicken Eggs after Infection with Spring-Summer Meningo-Encephalitis Virus] *Zent. f. Bakt. I. Abt. Orig.* 1960, v. 179, No. 2, 160-67, 3 figs.

A study has been made of the histological appearances in chick embryos infected with spring-summer meningo-encephalitis virus, a member of the tick-borne encephalitis group. After 13 passages on the chorioallantoic membrane the virus produced small proliferations on the ectoderm with parakeratosis and areas of necrosis passing down into the mesoderm, where they were surrounded by mesenchyme cells. The endoderm and yolk sac were unaffected. In the embryo the brain showed signs of encephalitis, with infiltrates and destruction of nerve tissue and large and small haemorrhages. The skeletal muscles were severely affected by necrotizing myositis. No abnormalities were observed in the heart, lungs and liver. The histological appearances are illustrated in photomicrographs, and resemble those produced in chick embryos by other viruses of the tick-borne encephalitis group. *D. J. Bauer*

PORTERFIELD, J. S., WILLIAMS, M. C. & WOODALL, J. P. **A Plaque Technique for the Primary Isolation of Arthropod-Borne Viruses.** [Correspondence.] *Nature.* 1960, Oct. 15, v. 188, 252-3.

During an epidemic of O'nyong-nyong fever in Uganda an acute-phase human serum from which virus had been isolated in suckling mice was sent to London where it was plated on a chick embryo monolayer culture [this *Bulletin*, 1960, v. 35, 86, 715]. 50 plaques were produced by a 1:10 dilution and 3-4 by a 1:100 dilution. 4 other sera from which virus was simultaneously isolated in suckling mice were tested on monolayers in Uganda and failed to produce plaques.

A small outbreak of Rift Valley fever was also investigated by both methods. Virus was isolated by both methods from 2 acute-phase human sera and from a mosquito suspension. *C. E. Gordon Smith*

ARAKAWA, S.; HOSHINO, J.; NAGASHIMA, H.; KANEKO, T.; SEKI, T.; SATO, T. **Experimental Study on Measles Virus. 4th Report: Adaptation of the Virus to Mouse-Brain, especially after Serial Passages through Chick Embryo Cultures** [ARAKAWA, HOSHINO, NAGASHIMA, KANEKO & SEKI]. *Arch. f.d. gesamte Virusforschung*. 1960, v. 9, No. 5, 647-55. [25 refs.] **5th Report: Immuno-Serological Examination of Mouse-Adapted Measles Virus** [ARAKAWA, HOSHINO, KANEKO & SATO]. *Ibid.*, 656-64, 4 figs. [14 refs.]

i. 6 strains of measles virus were isolated by egg passage followed by inoculation of mice. Serum taken from patients during the first 48 hours of illness was inoculated on the chorioallantoic membrane of fertile eggs at the 9th-10th day of incubation. Passage was made from the membrane after incubation at 36°C. for 4-5 days, and after 5-16 passages the material was pathogenic for 6-7 gm. mice on intracerebral injection.

ii. The identity of the strains after adaptation to mice was confirmed by serological tests with measles convalescent-phase sera. 75 of 107 patients suffering from measles developed antibodies fixing complement with antigen prepared from mouse brain infected with an adapted strain of measles virus, and the appearance of neutralizing antibody to the same strain was also observed. [For previous studies, see this *Bulletin*, 1954, v. 29, 1134.] *D. J. Bauer*

TOYOSHIMA, K.; TAKAHASHI, M.; HATA, S.; KUNITA, N.; OKUNO, Y. **Virological Studies on Measles Virus. I. Isolation of Measles Virus using FL Cells and Immunological Properties of the Isolated Agents** [TOYOSHIMA, TAKAHASHI, HATA, KUNITA & OKUNO]. *Biken's J.* Osaka. 1959, Dec., v. 2, No. 4, 305-12, 6 figs. (5 on 3 pls.) [14 refs.] **II. Growth of Toyoshima Strain in Four Established Cell Lines** [TOYOSHIMA, HATA, TAKAHASHI, KUNITA & OKUNO]. *Ibid.*, 313-20, 11 figs. (9 on 3 pls.)

A strain of measles virus (Toyoshima strain) could be isolated in the FL continuous line of human amnion cells from the throat washings of a patient suffering from measles collected at the time of onset of the exanthem. After 7 passages the virus attained a titre of 10^7 TCD₅₀/ml., and its identity was established in cross-serological tests with the Edmonston strain of measles virus. The infected cultures showed giant cells with eosinophilic intracytoplasmic and intranuclear inclusions. The virus also grew in HeLa cells and in continuous lines of human liver and conjunctival cells; although their susceptibility to infection was lower than that of FL cells by 2-3 log units, the 3 cell lines gave the same yield of virus as FL cells at the height of the cytopathic effect. *D. J. Bauer*

CABASSO, V. J., AVAMPATO, J. E., KISER, K. H. & STEBBINS, M. R. **Further Evidence of Immunologic Dissimilarity of Distemper (CD) and Measles (M) Viruses.** *Proc. Soc. Exper. Biol. & Med.* 1960, Aug.-Sept., v. 104, No. 4, 526-9. [17 refs.]

"Additional experimental evidence of dissimilarity of canine distemper (CDV) and measles (MV) viruses are presented: 1. Ferrets inoculated with repeated doses of MV-adjuvant mixture and which developed M antibodies proved as susceptible as control animals to challenge with CDV. 2. Paired convalescent sera from measles patients showed significant measles antibody rises, while CD antibodies remained essentially absent. 3. Growth of MV in HeLa cells was not inhibited by presence of CD antiserum or normal serum, while MV antiserum apparently reduced virus multiplication. Presence of measles antiserum did not interfere with propagation of CDV. 4. By 14th day after MV infection, serologically negative monkeys developed high antibody titers for MV but none for CDV. It remains to be determined whether results obtained are attributable to particular virus strains used, or apply also to other isolates of MV and CDV."

SCHWARZ, A. J. F.; BOYER, P. A.; ZIRBEL, L. W.; YORK, C. J.; HOEKENGA, M. T.; PALMA, H. C. **Experimental Vaccination against Measles. I. Tests of Live Measles and Distemper Vaccine in Monkeys and Two Human Volunteers under Laboratory Conditions** [SCHWARZ, BOYER, ZIRBEL & YORK]. *J. Amer. Med. Ass.* 1960, June 25, v. 173, No. 8, 861-7, 2 figs. [13 refs.] **II. Tests of Live Measles and Live Distemper Vaccine in Human Volunteers during a Measles Epidemic in Panama** [HOEKENGA, SCHWARZ, PALMA & BOYER]. *Ibid.*, 868-72, 2 figs.

I. The immune response to the administration of live measles vaccine prepared from the Edmonston strain of virus grown in tissue culture was studied in cynomolgus monkeys and human volunteers. The virus could be recovered between the 3rd and 15th days after administration from the throats of 3 and the blood of 2 of 4 monkeys given the vaccine by mouth, and after intramuscular injection the virus was recovered in 3 of 13 and 4 of 12 instances respectively. The monkeys showed no signs of illness, but all developed complement-fixing and neutralizing antibodies. 2 children aged 2½ and 4 years were given the vaccine intramuscularly; both developed a brief febrile illness with leucopenia after 7 days, but without a rash or Koplik spots, and both developed measles antibody. In similar studies carried out with live distemper vaccine all of 14 monkeys vaccinated intramuscularly or intracerebrally developed distemper complement-fixing and neutralizing antibodies, but there was no production of measles antibody, except for low complement-fixation titres in 2 animals. In 6 monkeys subsequently given measles vaccine no modification in the production of measles antibodies could be observed.

II. The measles vaccine was tested in 453 volunteers during an epidemic of measles in Panama in 1959. 70-80% of the children under 5 years of age [number not stated] developed a febrile illness after 6-10 days, and 50% developed a scanty macular exanthem. During the subsequent 4½ months 3 (0.7%) of the vaccinated persons developed measles, compared with 32 (9.0%) of 356 persons in an unvaccinated control group. 388

persons were also given distemper vaccine, and measles subsequently occurred in 14 (3.6%), and in 25 (6.0%) of a control group of 414 unvaccinated persons.

D. J. Bauer

FENJE, P. **Propagation of Rabies Virus in Cultures of Hamster Kidney Cells.** *Canadian J. Microbiol.* Ottawa. 1960, Oct., v. 6, No. 5, 479-84.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 191.]

WELLER, T. H., HANSHAW, J. B. & SCOTT, D. E. **Serologic Differentiation of Viruses responsible for Cytomegalic Inclusion Disease.** *Virology.* New York. 1960, Sept., v. 12, No. 1, 130-32.

A number of viruses have been isolated from human beings which cause cytopathic changes characterized by intranuclear inclusions and cytomegaly in cultures of

human fibroblasts. They include the so-called salivary gland (SG) viruses and cytomegalic inclusion (CI) disease viruses.

Cross-neutralization experiments, in human fibroblasts, done with sera from patients with CI disease against 1 strain of SG virus and several strains of CI disease virus showed greater neutralization with the homologous than heterologous strains, and indicated that the viruses belonged to several different serotypes. Some sera from cases of neonatal CI disease did not neutralize any of the antigens, suggesting either that they belonged to other antigenic types or that the infants had become tolerant to the virus *in utero* and so failed to make antibody to it. None of the neutralizing sera obtained from infants fixed complement with the antigens available, although the antigens gave good fixation with some sera from older children and adults. Attempts to make specific antisera in laboratory animals were unsuccessful.

It is proposed that the agents should be called the cytomegalovirus group, and 2 of the strains studied be designated types 1 and 2. (The reference to salivary glands is considered misleading as the viruses can be isolated from other tissues.)

Janice Taverne

IMMUNITY

FINNEY, D. J. **The Design and Analysis of an Immunological Assay.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 4, 341-68, 1 fig. [20 refs.]

Various methods have been proposed for analysing biological assays with a quantal response; that is, when the response consists in observing whether or not a particular phenomenon has occurred. The author illustrates these methods by applying them to an assay of typhoid vaccines, in which 3 different doses of each of 2 vaccines are administered to groups of mice, which are then exposed to a fixed challenge dose. The main conclusion drawn is that only the more complex methods such as probit analysis are generally reliable. Short-cut methods will frequently give accurate results, but at times may be very misleading. [This paper provides a very good account of the virtues and defects of alternative methods.]

P. Armitage

FERNANDEZ, N. A. **Serum Antibody Response of Malnourished Children as compared with Well Nourished Children.** *Bol. Asoc. Méd. de Puerto Rico.* 1960, July, v. 52, No. 7, 222-31, 1 fig. [22 refs.]

An attempt was made in Guatemala City to determine whether severe protein deficiency interferes with the production of antibodies. 10 children with kwashiorkor (already receiving high-protein diet) and 3 with marasmus were given 3 doses (each of 0.5 ml.) of TAB vaccine at

weekly intervals; serum samples, taken before vaccination and at weekly intervals for 5 weeks after the first dose, were examined for antibody titres against O and H antigens. 10 well-nourished children served as controls and 10 selected children from a typical Guatemalan village were simultaneously tested. The children with kwashiorkor proved as capable of producing antibodies as the well-nourished controls; a low antibody response was observed in the 3 marasmus cases; the village children gave a satisfactory response, slightly lower than that of the controls (an encouraging result, the author claims, for public health TAB vaccination programmes). No relation was found between antibody response, total serum proteins, serum albumin or serum globulin levels.

D. A. Cannon

CAMPBELL, D. H. & GARVEY, Justine S. **Factors involved in Antibody Formation.** *J. Infect. Dis.* 1960, July-Aug., v. 107, No. 1, 15-28, 4 figs. [Numerous refs.]

This paper, written as a *Festschrift* to Professor TALIAFERRO, is a discussion on the present-day theories of antibody formation, viz. (1) an adaptive or inductive enzyme mechanism, (2) the template theory, and (3) a mutation, with changes involving either DNA or RNA. Quoting 63 references (many of them composite) the authors discuss first the properties of antigen: the molecular weight is relatively high; antigen is "foreign" to the host; it is a natural product; it is digestible; and

very small portions of the whole antigen molecule are the active, functional groups in antibody formation. After a short section on the physical and biological properties of antibodies, the main section of the paper, on antibody formation, deals with the differences between primary and secondary responses, the role of adjuvants, antibody formation at the cellular level, simultaneous injection of antigen and antibody, the persistence of antigen, and its degradation and fragmentation. Concluding with a stimulating list of speculations, the authors think that "the mystery of antibody formation still confronts us", but also that "one cannot help sensing that the solution to the problem of protein synthesis and the role of antigen, or perhaps antigenic fragments, in the stimulation and modification of protein molecules, which we call antibody, is not far away".

D. A. Cannon

WATSON, K. C. **Observations on the Role of Immune Antibody in Protection in Enteric Infections.** *South African J. Lab. & Clin. Med.* 1960, June, v. 6, No. 2, 95-106. [46 refs.]

In this essay the author examines some of the published evidence concerned with the production of antibody and immunity in typhoid fever by means of various TAB vaccines and the natural disease itself and comes to the conclusion that the role played by specific antibody, either in the prevention of the disease by artificial means or recovery from the acute infection, is a limited one and suggests [without much evidence] that the "phagocytic defence mechanisms" are considerably more important.

[The selection of the literature quoted and the associated arguments are quite reasonable; they follow the same lines that are so familiar to all students of this particular subject. No original ideas are presented in this essay and although there seem to be some misunderstandings the article is of interest, but it cannot be regarded as a highly critical review of the subject.]

H. J. Bensted

CHIN, P. H. & SILVERMAN, M. S. **Studies on the Transfer of Antibody Formation by Iso- and Heterotransplants.** *J. Immunology.* 1960, Aug., v. 85, No. 2, 120-29, 4 figs. [30 refs.]

In this interesting but technically difficult paper (which experimental immunologists will want to read in the original), evidence is presented that the transfer of spleen cells, but not bone marrow cells, from immunized rats into lethally irradiated mice resulted in the transfer of antibody synthesis. Serum agglutinins were successfully demonstrated when either *Salmonella typhi* or sheep RBC were employed as antigens. The antibodies formed were shown to be synthesized by the transferred cells and not by the recipients. This antibody production by transplanted rat spleen cells suggests that a graft v. host immunological reaction appears to be possible when lymphoid tissue is transplanted; evidence was not obtained that such a reaction occurs with the transplantation of bone marrow cells.

D. A. Cannon

YAGI, Y., ENGEL, K. & PRESSMAN, D. **Quantitative Determinations of Small Amounts of Antibody by use of Solid Adsorbents.** *J. Immunology.* 1960, Oct., v. 85, No. 4, 375-86, 3 figs. [20 refs.]

GLEDHILL, A. W. & REES, R. J. W. **Effect of a Primary Tuberculous Infection on the Resistance of Male and Female Mice to Ectromelia** [Correspondence.] *Nature.* 1960, Aug. 20, v. 187, 703-4.

The resistance of mice and guinea-pigs to secondary infection by various bacteria has been shown to be increased by a primary tuberculous infection or vaccination with BCG. This paper reports experiments undertaken to see whether a primary tuberculous infection also increases resistance to virus infections. Under the conditions of these experiments, tuberculosis increased the resistance of adult male mice to the lethal effects of ectromelia, a typical pox virus. The resistance of normal female mice, initially higher than that of normal male mice, was not significantly influenced by a primary tuberculous infection. The lower resistance of the normal males compared with the females may not apply to mice of all strains and ages. It is not known whether this increased resistance to a virus infection (now for the first time reported) is due to the same non-specific immune processes which operate against bacterial infections.

D. A. Cannon

LEVY, M. N., BLATTBERG, B. & BARLOW, J. L. **Effect of Hemorrhagic Shock upon the Properdin System of the Dog.** *J. Lab. & Clin. Med.* 1960, July, v. 56, No. 1, 105-9, 1 fig.

Phage-neutralization can be used to observe a change in properdin level [BARLOW *et al.*, this *Bulletin*, 1958, v. 33, 992 *bis*]. In dogs subjected to the standard haemorrhagic shock procedure the complement and phage-neutralization titres were measured. Complement levels were not appreciably affected, but the phage-neutralization titre fell—not significantly in the oligoemic phase of shock, but to about half the control level in the terminal stage after transfusion had been completed. This is taken to be an indication of the impairment of the immunological defence mechanism in haemorrhagic shock.

D. A. Cannon

NORTH, E. A. & PAWLYSZYN, G. **Specific Immunity against *Staphylococcus* Infection in Mice not associated with Demonstrable Antibody in the Serum: Interference Effect.** *Med. J. Australia.* 1960, June 11, v. 1, No. 24, 925-9. [11 refs.]

Subcutaneous injection of mice with killed whole-cell staphylococcal vaccines gave some protective effect against intraperitoneal challenge with living cells 1 or 2 days after vaccination, but not 5 hours, nor 7 or more days, afterwards. Protection was also conferred by a heterologous strain of *Staph. aureus* and by a *Staph. albus*, but not by a streptococcus vaccine. It is suggested that the effect is similar to the interference effect demonstrated for *B. pertussis* by EVANS and PERKINS [this *Bulletin*, 1955, v. 30, 72].

R. E. O. Williams

GORDON, G. B. & KING, D. W. **Phagocytosis.** *Amer. J. Path.* 1960, Sept., v. 37, No. 3, 279-92. [33 refs.]

"Phagocytosis of carmine by L cells is an energy dependent process which may proceed under anaerobic conditions of short duration.

"Incorporation of Thorotrast is a non-energy dependent process most closely resembling a physical adsorption phenomenon.

"The role and possible mechanisms of phagocytosis are discussed."

JENKIN, C. & BENACERRAF, B. **In vitro Studies on the Interaction between Mouse Peritoneal Macrophages and Strains of *Salmonella* and *Escherichia coli*.** *J. Exper. Med.* 1960, Aug. 1, v. 112, No. 2, 403-17, 7 figs. [26 refs.]

There is a marked difference between the phagocytosis of virulent and avirulent strains of *Salmonella* which have been opsonized with normal mouse plasma: the virulent strain is never so well phagocytosed as the avirulent strain. Whereas the avirulent strain phagocytosed by the normal mouse peritoneal macrophages is killed, the virulent strain under such conditions remains viable and is able to multiply.

When, however, specific antiserum is used to opsonize the organisms, or even the non-specific plasma from mice infected with BCG, the effect of phagocytosis is quite different. Virulent strains of *Salmonella* are treated by normal mouse macrophages in the same way as avirulent strains; they are killed. Moreover virulent strains opsonized with BCG plasma are much more efficiently phagocytosed and killed by peritoneal macrophages from mice infected with BCG than by those from normal mice.

H. J. Bensted

JENKIN, C. & PALMER, D. L. **Changes in the Titre of Serum Opsonins and Phagocytic Properties of Mouse Peritoneal Macrophages following Injection of Endotoxin.** *J. Exper. Med.* 1960, Aug. 1, v. 112, No. 2, 419-29, 5 figs. [23 refs.]

Macrophages harvested from the peritoneal cavities of mice previously inoculated with endotoxin appear to be more efficient in phagocytosing homologous bacteria in the presence of serum opsonins than macrophages obtained from normal mice. Further examination has shown that the percentage of organisms phagocytosed and killed within the peritoneal cavity of the mouse is directly related to the opsonic titre of the mouse serum or mouse plasma. Thus the treatment of experimental animals with endotoxins derived from Gram-negative bacteria induces a state of non-specific immunity which depends on an increase in the titre of the serum opsonins and an increased phagocytic power to take up and kill bacteria [this *Bulletin*, 1960, v. 35, 524]. H. J. Bensted

BERK, R., NELSON, E. L. & PICKETT, M. J. **Studies on Mechanisms of Cellular Immunity. I. Observations on the Metabolism of Mouse Monocytes.** *J. Infect. Dis.* 1960, Sept.-Oct., v. 107, No. 2, 175-82. [18 refs.] **II. Observations on the Interaction of *Pseudomonas aeruginosa* with Various Mammalian Cells and Fluids.** *Ibid.*, 183-8.

RUTENBURG, S. H., SCHWEINBURG, F. B. & FINE, J. **In vitro Detoxification of Bacterial Endotoxin by Macrophages.** *J. Exper. Med.* 1960, Nov. 1, v. 112, No. 5, 801-7.

FREEDMAN, H. H. **Further Studies on Passive Transfer of Tolerance to Pyrogenicity of Bacterial Endotoxin. The Febrile and Leucopenic Responses.** *J. Exper. Med.* 1960, Oct. 1, v. 112, No. 4, 619-34, 6 figs. [44 refs.]

"The effect of various schedules for inducing tolerance to bacterial endotoxin in donor rabbits upon suitability for demonstration of passive transfer of tolerance to pyrogenicity in normal recipients has been investigated. Long-term treatment of donors, through 5 weeks, is no more effective than a brief series of injections, adding further evidence that tolerance is not attributable to specific antibody to the endotoxin. Qualitative differentiation of the febrile pattern of passively tolerant recipients from that seen in control animals depends upon the magnitude of the test dose of pyrogen.

"Passively tolerant rabbits respond to endotoxin with an acute leucopenia equivalent to that seen in controls suffering a full biphasic fever. Animals given daily injections of endotoxin continue to show the acute leucopenia, despite the early modification of the course of fever characteristic of endotoxin tolerance. The assumption that the leucopenia reflects damage to the leucocytes, with release of endogenous pyrogen, is not consistent with these findings. Rabbits rendered leucopenic by nitrogen mustard and then given endotoxin exhibit a rapidly developing fever of greater than normal intensity, the exaggeration of the febrile response being proportional to the severity of the induced leucopenia.

"The implications of these findings for the pathogenesis of endotoxin-induced fever are discussed. The evidence supports the hypothesis that endotoxin produces fever by direct action rather than by release of endogenous leucocytic pyrogen. It is postulated that the lesser fever, in animals having normal numbers of circulating leucocytes, reflects a limitation of available endotoxin by the known rapid sequestration in the white blood cells at the time of the acute leucopenia. It is further suggested that the biphasic febrile response of the normal rabbit results from reinoculation of the blood stream by the temporarily sequestered endotoxin, the RES of the tolerant animal clearing the released endotoxin at a rate sufficient to prevent triggering the second phase of fever."

Miscellaneous

beham
TUBERCLE. 1960, Aug., v. 41, No. 4, 290-301. [31 refs.]
Smoking and Chest Disease. Report of the
JOINT TUBERCULOSIS COUNCIL OF GREAT BRITAIN.

The Joint Tuberculosis Council is an independent body composed of representatives from various medical societies with an interest in tuberculosis and other diseases of the chest. It set up a special committee to review the relationship between smoking and various chest diseases and this report contains the considered opinion of the Committee and the conclusions of the Council. It is concluded that smoking, particularly of cigarettes, is a major factor accounting for the increased incidence of cancer of the lung, that it impairs ventilation of the lungs in healthy persons, that it is closely related to the development of chronic bronchitis and that it may be one of the causes of the breakdown of quiescent respiratory tuberculosis. It is recognized that other factors are also important in the production of these diseases, particularly atmospheric pollution.

The Council recommends a more active policy designed to reduce the amount of cigarette smoking. Special efforts should be made to discourage young people from taking up smoking and members of the medical profession should, by example and persuasion, assist their patients and others to reduce, or abandon, cigarette smoking.

Smokers of pipes or cigars do not appear to have the same amount of serious ill health as cigarette smokers, and the Council considers that a reduction in the cost of cigar and pipe tobacco would assist the change to the less harmful forms of smoking.

Richard Doll

Wig
WIGDERSON, A. & KOHAN, M. **Relationship of Smoking to Respiratory Complaints and Ventilatory Function.** *Canadian Med. Ass. J.* 1960, Sept. 10, v. 83, No. 11, 585-7.

113 men were studied to see if there was any relationship between smoking and respiratory complaints and ventilatory capacity. Data for 14 non-smokers and 12 smokers among men aged under 40 years employed by a hospital showed no difference in the proportions with respiratory complaints or with reduced ventilatory capacity. The data for 12 non-smokers and 29 smokers

among men aged 40-60 years employed by the same hospital showed a much higher proportion of men with respiratory complaints and a substantially higher proportion with reduced ventilatory capacity among the smokers. Data for 16 non-smokers and 30 smokers among men aged over 60 years in a home for the aged showed a higher proportion of men with respiratory complaints among the smokers but little difference in the proportion with reduced ventilatory capacity.

According to the authors, the findings suggest that smoking is related to respiratory complaints. The relationship with reduced ventilatory capacity appeared to be less marked, and the disturbances in ventilation were not found to progress with age. [See also this *Bulletin*, 1959, v. 34, 448; 1960, v. 35, 17, 533.]

Richard Doll

W
LOWE, C. R. **Smoking Habits related to Injury and Absenteeism in Industry.** *Brit. J. Preventive & Social Med.* 1960, Apr., v. 14, No. 2, 57-63, 6 figs.

Smoking habits of over 7,000 employees of a large factory were recorded at the time they attended for mass radiographic examination. A year later over 3,000 of the workers were still employed and an examination was made of their absenteeism and frequency of attendance at the first-aid room for minor injuries in relation to their smoking habits. The results showed that frequency of attendance for the treatment of injury was higher among smokers than among non-smokers and increased fairly regularly with the amount smoked. The relationship with smoking was practically limited to men aged under 35 years. Absenteeism for medical reasons was also higher among smokers than non-smokers and also increased with the amount smoked. In this case the relationship was practically limited to men aged 35 years and over. Absenteeism for non-medical reasons was unrelated to smoking habits. It is suggested that the relationship between absenteeism and smoking follows from the known relationship between smoking and diseases such as chronic bronchitis, peptic ulcer, etc. The explanation for the relationship with minor injuries might be that the sort of person who is prone to accidents is also inclined to take up smoking and to smoke more heavily.

Richard Doll

Book Reviews

GEFFEN, Dennis [O.B.E., M.D., D.P.H.], BROWN, L. Farrer [C.B.E., B.Sc.] & WARREN, Michael D. [M.D., D.P.H., D.I.H.]. **Public Health and Social Services**. 5th Edition. 164 pp. 1960. London: Edward Arnold (Publishers) Ltd., 41, Maddox Street, W.1. [10s. 6d.]

The first edition of this popular book appeared in 1940 when the authors were Dr. Geffen and Mr. Farrer Brown. Since the publication of the 4th edition 3 years ago, Dr. Geffen has unfortunately died and Dr. Warren of the London School of Hygiene and Tropical Medicine has joined Mr. Farrer Brown in bringing out this latest edition.

Recently there has been considerable development in many sections of the public health field, especially in the promotion of mental health and in services for deprived children and the aged, and there has been closer appreciation of the value of trained social workers in many branches of public health. All these are adequately covered in this new edition.

The book is still small—it can be slipped easily into a coat pocket or a handbag—but it is remarkably complete. It is up-to-date and contains references to the report of the Cranbrook Committee and to the recent increase to 15 in the number of Regional Hospital Boards, but there is no mention of the fairly new term, perinatal mortality, which midwives ought to know about.

Nevertheless it is well balanced, clearly written with economy of words and is eminently suited for pupil midwives and midwives, for whom it was originally intended. It will, in fact, be useful to all who wish to acquire knowledge of how the health services work and what they are trying to do.

The volume is singularly free from typographical errors but "a bacteria" occurs 3 times and in the "List of Useful Addresses" that of the Ranyard Nurses should be Kennington Road, and the present, instead of the former, address of the Royal College of Midwives should be given.

The index is very good.

Allen Daley

WILLIAMS, R. E. O. [M.D., M.R.C.P.], BLOWERS, R. [M.D.], GARROD, L. P. [M.D., F.R.C.P.] & SHOOTER, R. A. [M.D.]. **Hospital Infection, Causes and Prevention**. pp. x + 307, illustrated. 1960. London: Lloyd-Luke (Medical Books) Ltd., 49, Newman Street, W.1. [35s.]

In their preface the authors state with reference to recent investigations into hospital infection, that "it would be helpful to present a coherent account of all this work in a single volume, with emphasis both on the epidemiology of the various infections and on such practical recommendations as the facts seem to justify". This statement admirably describes the scope of this book, which is in two parts: in the first the epidemiology

of hospital infection is discussed, and in the second its control.

The first part consists of separate chapters on various types of infection, streptococcal, with Gram-negative organisms, gastro-intestinal diseases, urinary tract infections, tetanus and gas gangrene and other infections. There are 3 chapters devoted to the important topic of staphylococcal infection: a general introduction, infection in maternity units and surgical sepsis. Each chapter contains an initial review of the available literature together with the opinions of the authors—the two always being clearly distinguishable. The general principles of prevention are also discussed in these chapters and there is a valuable short chapter on factors influencing the occurrence of infection.

In the second part different aspects of the control of hospital infection are described, again as a nicely balanced mixture of a review of published work and a discussion of it. An introductory chapter on the administrative control of hospital infection deals with the definition of sepsis, methods of assessing sepsis rates and the duties of the Control of Infection Officer. There is a detailed chapter on operating theatre design which would be of value to any who have the responsibility of planning for new hospitals or hospital reconstruction—the discussion on ventilating and heating being particularly helpful. In the chapter on ward infection detailed advice is given on ward hygiene, segregation of patients, the management of symptomless carriers and many individual ward procedures.

There are chapters on the use of antibiotics, on sterilization by heat, and on chemical disinfectants. The last reflects the current lack of precise information about the relative merits of the many disinfectants now available. A very useful chapter deals individually (and alphabetically) with the various items in a hospital that need to be sterilized or disinfected. The advice given cannot be based in every case on scientific evidence, because little exists, but all the suggestions are simple, practical and sensible, and this will undoubtedly be found to be one of the most frequently consulted chapters in the book.

Control of Infection Officers, pathologists and others who may be called to investigate outbreaks will find the chapter on this subject detailed and helpful: particularly useful is the detailed "check list" of things to be considered when making an investigation.

The final chapter deals with special technical methods, such as air sampling, phage-typing and the collection and bacteriological investigation of various sorts of specimens from hospitals.

The book is well produced and the style is most readable and not without humour. There is a wealth of references and each chapter closes with a bibliography.

It can be said with confidence that the authors have achieved what they set out to do and that this volume does in fact provide a coherent account of what is known at the present day about this subject. All who work in this field or have administrative responsibility for the control of hospital infection should read this book—and a copy should be available in every hospital for reference.

J. C. Kelsey

HIMMELWEIT, F. [M.D., Ph.D., F.R.C.P.] [Compiled and edited by], with the assistance of Martha MARQUARDT and under the editorial direction of Henry DALE, O.M., G.B.E., F.R.S., M.D., F.R.C.P. **The Collected Papers of Paul Ehrlich in Four Volumes including a Complete Bibliography. Vol. II. Immunology and Cancer Research.** pp. viii + 562, illustrated. 1957. **Vol. III. Chemotherapy.** pp. viii + 615, illustrated. 1960. London. New York. Paris. Oxford: Pergamon Press Ltd., Headington Hill Hall. [£8 each.]

The publication of volumes 2 and 3 of Ehrlich's collected papers [for volume 1 see this *Bulletin*, 1957, v. 32, 715] allows us to follow the majestic progress of his genius. The greater part of the second volume is given over to his researches into immunity which must surely be one of the most astonishing achievements in the history of medical research. We are able to understand the working of the mind of the master as he disentangles the action of antitoxin and builds up his famous side-chain theory. We watch him as he goes about the standardization and titration of antitoxin in much the same way as he would probe a question in physical chemistry. We might almost be looking over his shoulder as he doles out drops of toxoid into test tubes or draws his neat diagrams on his everlasting strips of coloured paper. So very chemical, it must surely have seemed, yet Ehrlich never lost grip with the biological background of immunity. Perhaps his relative Carl WEIGERT, a brilliant microscopist and innovator of many staining dyes, insisted upon that! At least one of Weigert's fertile ideas—the overproduction theory—was utilized in explaining the liberation of antitoxin from its formative cells.

6 papers on lysin action, published over the incredibly short period of 1899–1901, and culminating in his masterly Croonian Lecture to the Royal Society, built up the almost complete theory of immune body and complement. Then came far-reaching papers on receptors of red corpuscles, toxoid production with diphtheria toxin, multiplicity of complement and amboceptor action, each of which has played its part in establishing the side-chain theory and meeting the objections of distinguished anta-

gonists. With the Herter Lectures of 1904 we stand with Ehrlich on a lofty peak of genius and survey the promised land. This volume concludes with the papers on transplantable mouse tumours and the idea of athreptic immunity which still holds an important place in cancer research.

The third volume switches us over to chemotherapy. The papers are clearly fitted into 3 groups, of which the first includes the early studies on dye action on the malarial parasite and on trypanosomes, internal antiseptics and the chemotherapy of infectious diseases. Now comes the great dictum of chemotherapeutics that a drug must be parasitotropic without being too organotropic. And now, too, loom up the arsenical compounds with special attention being paid to arsanic acid and its reduction products.

The second group of papers is devoted to Salvarsan and Neosalvarsan and the treatment of syphilis, spirillosis and sleeping sickness. Toxic manifestations of these chemotherapeutic agents are admitted and constructively dealt with; some deaths after Salvarsan are reported.

"The collection in this volume of all that he published, dealing with all the investigation in this connexion which he himself performed, or in which he participated, should offer a new opportunity for the study and appreciation of the real magnitude of his achievement" writes Sir Henry Dale and we can only echo this admirable citation.

The volume concludes with last studies and reviews on chemotherapy, syphilis, arsenometallic combinations and the problems and controversies connected with the introduction of Salvarsan and the progressive development of its use. And finally, Ehrlich's obituary notices and tributes on Weigert, Albrecht, Robert Koch, Apolant and Bertheim show us another side of one whom we are apt to dissociate from the personal relationships of the family and the Institute.

If anything further were needed to make this noble enterprise a memorable success, it has been provided in the form of Sir Henry Dale's introduction. These storehouses of wisdom and warm-hearted personal recollection must surely be unique. The editorial staff and the publishers are, indeed, to be congratulated on a splendid achievement.

Roy Cameron